EXHIBIT B

United States Senate
Senate Finance Committee

Charles E. Grassley, Chairman
Ron Wyden, Ranking Member

Insulin:

Examining the Factors Driving the Rising Cost of a Century Old Drug

Staff Report

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I. Introduction

On January 22, 2019, Chairman Grassley and Ranking Member Wyden sent a letter to Sanofi, Eli Lilly, and Novo Nordisk requesting information relating to the process by which they price their insulin products.[1] A few months later, on April 2, 2019, Chairman Grassley and Ranking Member Wyden sent letters to CVS Caremark, OptumRx, and Express Scripts requesting information about how their role within the insulin market impacts the cost of insulin drugs.[2] These letters began the Chairman's and Ranking Member's insulin investigation. This investigation aimed to shed light on how drug manufacturers price insulin medication, the role played by pharmacy benefit managers (PBMs), and the financial and contractual relationships between these entities.

Relatively little is publicly known about these financial relationships and the impact they have on insulin costs borne by consumers, even though PBMs play a major role in the drug supply and payment chain by negotiating drug rebates and discounts with manufacturers and managing drug benefits for health care payers, including private insurers, employers, and entities that provide coverage under Medicare, Medicaid, and the Children's Health Insurance Program (CHIP). The Senate Finance Committee has jurisdiction over these Federal health care programs and thus has an obligation to inform other members of Congress and the public of these interactions and how they affect drug prices.

This investigation builds on work that Chairman Grassley and Ranking Member Wyden have conducted in recent years to shed light into the prescription drug supply chain, and their joint and individual efforts to bring accountability to those responsible for rising drug prices.[3] For almost two years, investigative staff reviewed more than 100,000 pages of internal company documents produced by Sanofi, Novo Nordisk, Eli Lilly, CVS Caremark, Express Scripts,

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[1] Press release, Grassley, Wyden Launch Bipartisan Investigation into Insulin Prices (Feb. 22, 2019), https://www.grassley.senate.gov/news/news-releases/grassley-wyden-launch-bipartisan-investigation-insulin-prices.

[2] Press release, Grassley, Wyden Question Role of Middlemen in Skyrocketing Insulin Prices (Apr. 2, 2019), https://www.grassley.senate.gov/news/news-releases/grassley-wyden-question-role-middlemen-skyrocketing-insulin-prices.

[3] In 2015, Ranking Member Wyden and Senator Grassley, who was then-Chairman of the Senate Judiciary Committee, released the findings of an 18-month long investigation into the pricing of Sovaldi and Harvoni, new "blockbuster" hepatitis C therapies whose price caused an international uproar. *See* Press release, Wyden-Grassley Solvaldi Investigation Finds Revenue-Driven Pricing Strategy Behind $84,000 Hepatitis Drug (Dec. 2015), https://www.finance.senate.gov/ranking-members-news/wyden-grassley-sovaldi-investigation-finds-revenue-driven-pricing-strategy-behind-84-000-hepatitis-drug. In 2018, Ranking Member Wyden released a report detailing a year-long Minority staff investigation that used public documents to explain the path that a prescription drug takes from the lab bench to the medicine cabinet or doctor's office. *See* Press Release, Wyden Releases Report on High Drug Prices in Medicare (June 2018), https://www.finance.senate.gov/ranking-members-news/wyden-releases-report-on-high-drug-prices-in-medicare. In 2019, the Senate Finance Committee held three hearings on drug pricing, bringing executives from drug companies and PBMs to testify before Congress and released the Prescription Drug Price Reduction Act (PDPRA) of 2019 in an effort to shed light on drug manufacturers pricing practices and bring down drug costs for seniors. In 2020, Chairman Grassley and Ranking Member Wyden released a bipartisan report to Finance Committee colleagues detailing how opioid manufacturers use tax-exempt organizations as extensions of their sales and marketing strategy. *See* Press release, Grassley, Wyden Call for Greater Drug Industry Transparency in Report Exposing Opioid Makers' Ties to Tax-Exempt Groups (Dec. 2020), https://www.finance.senate.gov/chairmans-news/grassley-wyden-call-for-greater-drug-industry-transparency-in-report-exposing-opioid-makers-ties-to-tax-exempt-groups.

OptumRx as well as documents and data produced by the Centers for Medicare and Medicaid Services (CMS). Investigative staff also met with experts with knowledge of the United States' drug pricing system and interviewed individuals within OptumRx and Express Scripts who have direct knowledge of how insulin is priced within their respective companies.

Information and documents collected during the course of this investigation suggest that a combination of factors contributed to consumers facing higher costs for insulin over the last 15 years. First and foremost, pharmaceutical manufacturers have complete control over setting the list price (the Wholesale Acquisition Cost (WAC)) for their products. This investigation found that manufacturers aggressively raised the WAC of their insulin products absent significant advances in the efficacy of the drugs.[4] These price increases appear to have been driven, in part, by tactics PBMs employed in the early 2010s. At that time, PBMs began to more aggressively pit manufacturers against each other by implementing formulary exclusions in the insulin therapeutic class, which effectively stopped manufacturers from reaching large blocks of patients. While insulin manufacturers had been increasing prices for their products prior to formulary exclusions being employed, this tactic appears to have been more effective in boosting the size of rebates than suppressing the upward march of WAC prices. As a result, pharmaceutical manufacturers continued to raise WAC prices aggressively—increases that were often closely timed with price changes made by competitors (a practice that has been referred to as "shadow pricing").

The Finance Committee found that drug manufacturers increased insulins' WAC in part to give them room to offer larger rebates to PBMs and health insurers, all in the hopes that their product would receive preferred formulary placement. This pricing strategy translated into higher sales volumes and revenue for manufacturers. In some cases, manufacturers appear to have been concerned that decreasing WAC prices would be viewed negatively by PBMs, since PBMs capture a portion of rebate revenue and are also paid administrative fees based on a percentage of WAC.

This report describes how Sanofi, Novo Nordisk, and Eli Lilly set the price for their insulin drugs and how those decisions were affected not only by their competitors' pricing decisions, but also by their perceived need to offer large rebates, discounts, and other fees to PBMs such as CVS Caremark, OptumRx and Express Scripts and other payers. In addition, this report also discusses and analyzes the financial and budgetary impacts of insulin on both private and public payers, including Medicare and Medicaid. Lastly, this report discusses and analyzes rebate agreements executed between manufacturers and PBMs, and seeks to shed light on the role PBMs play in the U.S. drug pricing system.

[4] Insulin manufacturers appear to focus their R&D efforts on new insulin-related devices, equipment, and other mechanical parts which are separate from insulin's formulation. For example, in response to the Committee's request for information, Sanofi listed all patents received by the company since January 1, 2014. Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, on Behalf of Sanofi, to Senator Grassley and Senator Wyden (Mar. 8, 2019). Most, if not all, of these are patents for pen-type injectors or drive mechanisms used in drug delivery devices. (Sanofi's patent on insulin expired in 2014, paving the way for others to utilize Sanofi's insulin glargine formulation). This suggests that manufacturers' R&D spending is primarily focused on insulin-related devices, rather than insulin itself.

II. Key Findings

1. **The WAC prices of long- and short-acting insulins have risen steeply.** Sanofi's long-acting insulin pens, Lantus SoloStar, increased from $303 in 2014 to $404 in 2019. The WAC price of Novo Nordisk's long-acting insulin pens, Levemir FlexTouch, increased from $303 in May 2014 to approximately $462 in January 2019, representing an increase of $159—or 52%— in a little more than five years. Eli Lilly's rapid-acting insulin, Humalog 50-50 Kwikpen, had a WAC of $530 in 2017 compared to $323 in 2013—an increase of $207 or 64% in four years. Sanofi's rapid-acting insulin, Apidra Solostar, also increased—from $302 in 2014 to $521 in 2019—while Novo Nordisk's rapid-acting insulin, Novolog FlexPen, rose from $324 in 2013 to $558 in 2018, representing a more than 70% WAC price hike for both companies during this time period.

2. **Spending on insulin products has increased significantly for the Medicare program and its beneficiaries.** Based on data collected from CMS, annual spending on insulin has increased by billions of dollars over the last decade. Between 2010 and 2018, Medicare Part D spent $78.4 billion on insulin, prior to rebates, the majority of which was spent on Lantus ($27.4 billion), Novolog ($16.5 billion), Humalog ($12.3 billion), and Levemir ($11 billion). The growth of CMS's pre-rebate spending on insulin also significantly outstripped the growth rate of beneficiaries utilizing insulin from 2010 to 2018. For instance, the number of Part D beneficiaries using insulin increased 51%, from over 2.1 million in 2010 to approximately 3.2 million in 2017, whereas spending on insulin prior to rebates increased more than 470%, from over $3 billion in 2010 to roughly $14.3 billion in 2018.

3. **Sanofi aggressively increased its list price between 2012 and 2014 in response to market pressure and competition.** From 2001 to 2012, Sanofi increased list price as much as 18% annually, raising its price from $34 to $131 by the end of 2012. However, in 2013 and 2014, Sanofi embarked on much more aggressive increases, nearly doubling the drug's WAC to $248 by the end of 2014. Internal documents suggest that Sanofi did this for three reasons: (1) to lock in price increases in advance of introducing a new insulin product called Toujeo and anticipated market competition from Eli Lilly, (2) to respond to aggressive rebate and discount activity from Novo Nordisk, and (3) to respond to increased pressure from PBMs and payers to offer large rebates and discounts.

4. **Novo Nordisk repeatedly tracked Sanofi's price increases in a practice known as "shadow pricing."** Rather than seeking to undercut its competitors' pricing, from 2014 on Novo Nordisk engaged in a cat-and-mouse strategy of pricing that followed Sanofi's price increases closely, sometimes mirroring them within days or even hours. In 2015, Novo Nordisk changed its pricing strategy in advance of launching Tresiba, its next generation basal insulin (also known as long-acting insulin). Instead of following Sanofi, it led with a list price increase in order to set a high basal insulin price floor from which to launch Tresiba's initial list price. However, in 2017 and

2018, Novo Nordisk resumed increasing its list price to respond to Sanofi's pricing actions. According to internal memoranda, on October 1, 2017, Sanofi increased Lantus's list price by 3% and Toujeo's list price by 5.4%. Roughly three weeks later, Novo Nordisk recommended that the company make a 4% list price increase on January 1, 2018 in response to Sanofi, which was approved as recommended on November 3, 2017. Novo Nordisk would make at least one more list price increase in response to Sanofi in 2018.

5. **Novo Nordisk's board of directors voted down a proposed insulin price decrease due to financial downsides, risk of backlash from PBMs and payers, and expected pressure to take similar action on other products.** PBMs and payer backlash appeared to be of particular concern to Novo Nordisk. The company believed that its decision to decrease list price could upset payers, and that many in the drug supply chain (e.g., wholesaler distributors, PBMs, and health insurers) would be negatively impacted financially and could retaliate against Novo Nordisk.

6. **Insulin R&D spending was a fraction of manufacturers' revenue and sales and marketing expenses.** Eli Lilly reported spending $395 million on R&D costs for Humalog, Humulin, and Basaglar between 2014 and 2018, during which time the company spent nearly $1.5 billion on sales and marketing expenses for its insulins. These three drugs generated $22.4 billion in revenue during that period. Similarly, Sanofi reported net sales of nearly €31 billion (approximately $37 billion based on current currency conversion rates)[5] between 2014 and 2018 for its five insulin products, during which time the company reported spending $902 million on insulin R&D. Novo Nordisk failed to provide requested R&D spending information to the Committee.

7. **Rebates for insulins have increased exponentially since 2013.** In July 2013, Sanofi offered rebates between 2% and 4% for preferred placement on CVS Caremark's client's commercial formulary. Five years later, in 2018, Sanofi rebates were as high as 56% for preferred formulary placement. Similarly, in 2017, Novo Nordisk offered Express Scripts up to a 47% rebate for Levemir for preferred formulary placement on their client's commercial formulary compared to 25% in 2014.

8. **Manufacturers are retaining more revenue from insulin than in the 2000s.** Data and documents produced to the Committee show that the amount of revenue pharmaceutical manufacturers are retaining from insulin has risen. The increased revenue is taking place even as the net price—the revenue after rebates and discounts—has declined in recent years, although it appears to remain significantly higher than in the first decade of the 21st Century. For example, Eli Lilly reported that the average net price for Humalog KwikPen had declined slightly from $28 per pen in 2015 to $24 per pen in 2018, despite the WAC price nearly doubling during that same period. Eli Lilly has reported a steady increase in Humalog revenue for more than a decade—from $1.5 billion in 2007 to $3 billion in 2018. An internal Sanofi presentation shows that while the average Lantus net price of $87.48 in 2016 was $32

[5] Sanofi reported net sales in Euros to the Securities and Exchange Commission.

lower than the drug's net price in 2014, it was roughly double the drug's net price of $46.92 in 2005.

9. **The three largest PBMs—CVS Caremark, Express Scripts, and OptumRx—command significant market power when negotiating rebates in comparison to smaller rivals.** PBMs and health plans with more bargaining power (i.e., those with more plan members) generally command higher rebates than those with less bargaining power (i.e., fewer members). For example, in 2014, Novo Nordisk offered WellPoint, the largest for-profit managed health care company with over 40 million members, a larger rebate (40.625%) for Novolin vials for preferred formulary placement as 1 of 2 manufacturers on their client's commercial formulary compared to North Carolina State Employees (27.625%). Similarly, Eli Lilly prepared widely divergent rebate bids within a few months of each other for Humulin and Humalog to a commercial health plan in Puerto Rico called SIS (22%), Cigna (45%-55% depending on formulary placement), a PBM in Puerto Rico called Abarca Health (up to 54%), and Optum's Part D business (68%).

10. **PBM contracting practices did little to discourage higher list prices for insulin.**

    a. **Exclusion lists.** When a drug is not included on a health plan's formulary, it is "excluded." Over the past decade, payers and PBMs have increased their use of formulary exclusion lists. Exclusion can have significant consequences for patients and manufacturers. For patients, if the drug is excluded, they are forced to either switch to a new product, which could affect adherence and health outcomes, or pay significantly more to stay on their preferred medication. For manufacturers, exclusion can result in significant financial loss and reduced market share. On the contrary, being the exclusive therapy on a formulary can also be advantageous for the manufacturer's market share and revenue, which incentivizes manufactures to offer larger discounts to maintain preferred status. This investigation found several instances where manufacturers increased their rebate offers significantly following the threat of exclusion. Furthermore, in instances when manufacturers considered decreasing the list price of their products, they ultimately decided against it in part because they believed PBMs and payers would react negatively to receiving smaller rebates and administrative fees by excluding their product.

    b. **Administrative Fees.** PBMs earn administrative fees from manufacturers each time a drug is dispensed at the pharmacy. Administrative fees vary by contract, ranging up to 5% of the WAC price for the insulin therapeutic class. These fees are a significant revenue stream for PBMs and likely act as a countervailing force against lower list prices—PBMs may be reluctant to push for lower WAC prices since it would reduce their administrative fee-based revenue. The Committee's investigation found several instances in which manufacturers decided against lowering their list price in fear of retaliation from PBMs and payers for this very reason.

c. **Price Protection.** In addition to rebates and administrative fees, PBMs negotiate contract terms in which payers receive an additional rebate when manufacturers increase their price beyond a certain percentage cap—referred to as price or inflation protection. Price protection terms vary from contract to contract. For example, they can cap the annual increase of a drug's WAC price increase (i.e. prior to rebates) or its net price (after rebates). The Committee found examples of annual price caps ranging from 0% to 12% in one contract alone. The Committee's investigation also found examples of manufacturers seeking to and succeeding in efforts to avoid paying these additional rebates by timing their WAC price increases to exploit the terms in PBM contracts.

III. Diabetes: The Disease and How It's Treated

Diabetes is among the most pervasive, deadly, and costly diseases in the United States. According to the Centers for Disease Control and Prevention (CDC), diabetes is the 7th leading cause of death in the U.S. and more than 34 million people in the country live with the disease.[6] Of these, 7.3 million adults were not even aware of, or reported, having diabetes.[7] The CDC also estimates that 88 million Americans have prediabetes, a health condition that can lead to type 2 diabetes.[8] Unfortunately, this trend does not appear to be slowing: the CDC estimates that 1.5 million Americans will be diagnosed with diabetes this year alone.[9]

The number of diabetes patients in the U.S. has grown steadily since 1958, when approximately 1.6 million people were diagnosed with the disease.[10] According to the International Diabetes Foundation, the U.S. has one of the highest per capita rates of diabetes in the world, and spends heavily on the disease in comparison to other countries.[11] Moreover, as the prevalence of diabetes continues to increase in the U.S., so does spending on the disease. According to the American Diabetes Association (ADA), the U.S. spent approximately $327 billion on diabetes in 2017, of which $237 billion represented direct health care expenditures related to the disease.[12] By comparison, the U.S. spent approximately $205 billion on diabetes in 2007 (in inflation-adjusted dollars).[13]

However, the disease burden of diabetes is not equally distributed in the United States. Diabetes has a major impact on Federal health care programs within the Finance Committee's jurisdiction, as well as the health and financial well-being of program enrollees. For instance, diabetes disproportionally impacts individuals enrolled in Federal health care programs, as the growth of diabetes is primarily among those 65 and older.[14] According to CMS, diabetes affects approximately 1 in 5 individuals enrolled in Medicare compared to about 1 in 10 in the general population.[15] Medicare beneficiaries with diabetes also "reported worse general health, more inpatient admissions, and higher out-of-pocket health care costs than those without diabetes."[16]

Diabetes prevalence also varies by geography, economic status, education level, and by ethnicity. Diabetes is significantly more prevalent in impoverished regions of the U.S. that have high rates of Medicaid enrollment such as Appalachia and the Mississippi Delta, as well as

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[6] CENTERS FOR DISEASE CONTROL AND PREVENTION, NATIONAL DIABETES STATISTICS REPORT (2020), https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf.
[7] *Id.*
[8] *Id.*
[9] *Id. See also Statistics About Diabetes*, AMERICAN DIABETES ASSOCIATION (ADA), https://www.diabetes.org/resources/statistics/statistics-about-diabetes (last viewed Nov. 18, 2020).
[10] CENTERS FOR DISEASE CONTROL AND PREVENTION, LONG TERM TRENDS IN DIABETES (2017), https://www.cdc.gov/DIABETES/statistics/slides/long_term_trends.pdf.
[11] International Diabetes Foundation Atlas, Table 3.5, Table 3.23 (2019), https://www.diabetesatlas.org/upload/resources/material/20200302_133351_IDFATLAS9e-final-web.pdf.
[12] American Diabetes Association, *Economic Costs of Diabetes in the U.S. in 2017*, 41 DIABETES CARE 917 (May 2018), https://care.diabetesjournals.org/content/41/5/917.
[13] *Id.*
[14] *Id.*
[15] *Diabetes Occurrence, Costs, and Access to Care among Medicare Beneficiaries Aged 65 Years and Over*, CTRS. FOR MEDICARE AND MEDICAID (Sept. 2017), https://www.cms.gov/Research-Statistics-Data-and-Systems/Research/MCBS/Downloads/Diabetes_DataBrief_2017.pdf.
[16] *Id.*

among people who are eligible for both Medicare and Medicaid (so called "dual eligible" beneficiaries).[17] Adults with less than a high school education are also more likely to be diagnosed with diabetes than those who have attained a high school education or greater.[18] Lastly, minority communities are also disproportionally affected by this disease, with American Indians, Hispanics, Black Americans, and Asian Americans representing more than 45% of those diagnosed with the disease,[19] despite these groups making up 39% of the U.S. population.[20] According to the CDC, 15.1% of American Indians, 12.7% of Hispanics, 12.1% of Black Americans, and 8% of Asian Americans have been diagnosed with diabetes.[21]

Rising insulin prices negatively impact Federal health care programs, private payers, and the health system as a whole, as payers bear the costs of inadequate treatment. (Proper glycemic control, achieved through medication use, can reduce health care costs of individual patients as well as hospital admissions.)[22] They also harm patient health by reducing access to this life-saving medication. Therefore, it is incredibly important for Congress to continue to study the root cause of diabetes and how the list price of insulin can serve as a barrier for diabetics to access the very medication that allows them to survive.

a. Diabetes: The Disease

Even though diabetes is the 7th leading cause of death in the U.S. (as of 2017), it is a treatable disease and has been for almost a century.[23] Prior to the discovery of insulin in 1921,

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[17] CTRS. FOR DISEASE CONTROL AND PREVENTION, DIABETES 2019 REPORT CARD (2019), https://www.cdc.gov/diabetes/pdfs/library/Diabetes-Report-Card-2019-508.pdf; CTRS. FOR MEDICARE AND MEDICAID SERVS., RACIAL AND ETHNIC DISPARITIES IN DIABETES PREVALENCE, SELF-MANAGEMENT, AND HEALTH OUTCOMES AMONG MEDICARE BENEFICIARIES (Mar. 2017), https://www.cms.gov/About-CMS/Agency-Information/OMH/research-and-data/information-products/data. *See also* Heather Landi, *Lessons Learned From the Mississippi Delta, Tackling Chronic Disease Through Remove Monitoring Technology*, HEALTHCARE INNOVATION (Oct. 3, 2016), https://www.hcinnovationgroup.com/population-health-management/.

[18] *Addressing Health Disparities in Diabetes*, CDC, https://www.cdc.gov/diabetes/disparities.html (last reviewed Apr. 15, 2019).

[19] CENTERS FOR DISEASE CONTROL AND PREVENTION, NATIONAL DIABETES STATISTICS REPORT (2020), https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf.

[20] *Quick Facts*, U.S. CENSUS BUREAU, https://www.census.gov/quickfacts/fact/table/US/PST045219 (last viewed Nov. 16, 2020).

[21] *Addressing Health Disparities in Diabetes*, CDC, https://www.cdc.gov/diabetes/disparities.html (last reviewed Apr. 15, 2019).

[22] *Cost-effectiveness of Intensive Glycemic Control, Intensified Hypertension Control, and Serum Cholesterol Level Reduction for Type 2 Diabetes*, JAMA NETWORK (May 15, 2002), https://jamanetwork.com/journals/jama/fullarticle/194927; *Medicaid Eligibility Expansions May Address Gaps In Access To Diabetes Medications*, HEALTH AFFAIRS (Aug. 2018), https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2018.0154.

[23] CENTERS FOR DISEASE CONTROL AND PREVENTION, NATIONAL DIABETES STATISTICS REPORT (2020), https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf. *See also The History of A Wonderful Thing We Call Insulin*, ADA (July 1, 2019), https://www.diabetes.org/blog/history-wonderful-thing-we-call-insulin. Despite being patented more than a century ago, insulin lacks a less expensive alternative in the United States that would introduce downward price pressure in the marketplace. In addition to list price and rebate dynamics discussed throughout this report, another reason for this situation is that insulin is a biologic—a product derived from living cells (e.g., plant, animal, human cells)—which makes it a complex drug molecule and difficult to manufacturer on a mass scale. For further reading, *see* Jeremy A. Greene & Kevin R. Riggs, *Why Is There No Generic Insulin? Historical Origins of a Modern Problem*, 372 N. ENG. J. MED. 1171 (2015). *See also What Are*

diabetes was difficult to manage, and was treated primarily with highly restrictive diets, which compromised immune systems, stunted growth, and could lead to death by starvation.[24] It wasn't until the late 19th and early 20th century that scientists began to understand the role that insulin and the pancreas play in diabetes.[25]

Diabetes occurs when the body cannot produce insulin (type 1) or use insulin properly (type 2), resulting in higher-than-normal levels of sugar in the bloodstream.[26] Insulin injections are the cornerstone of treatment for many people with diabetes, and patients depend on them to avoid severe health complications and death. The body uses carbohydrates, proteins and fats as sources of energy to function. Primarily, the body breaks down carbohydrates for energy, producing glucose.[27] As glucose levels rise in the bloodstream, the pancreas releases the hormone, insulin. Insulin moves glucose from the blood into the cells, where it can be used as a source of energy.[28] Without insulin, glucose accumulates in the blood stream leading to high blood sugar (or hyperglycemia).

More than 90% of people with diabetes are diagnosed with type 2.[29] Type 2 diabetes is a disease that can often be prevented and managed through diet and exercise.[30] However, if these interventions fail, medication is required for proper glycemic control. And, while this type of diabetes is often associated with older adults, children, teens, and young adults with obesity and other risk factors are also susceptible.[31] For type 2 diabetes, patients are treated with a variety of medications to manage their disease, most of which work by stimulating insulin production, improving the way the body absorbs sugar and uses insulin.[32] In contrast, Type 1 diabetes is an autoimmune endocrine disorder that can be diagnosed at any age, but more often presents in children, teens, and young adults.[33] Unlike Type 2 diabetes, Type 1 diabetes cannot be prevented

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"Biologics" Questions and Answers, FDA, https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/what-are-biologics-questions-and-answers (last viewed Oct. 6, 2020).

[24] *The History of A Wonderful Thing We Call Insulin*, ADA (July 1, 2019), https://www.diabetes.org/blog/history-wonderful-thing-we-call-insulin.

[25] CONG. RES. SERV., INSULIN PRODUCTS AND THE COST OF DIABETES TREATMENT (Nov. 19, 2018), https://fas.org/sgp/crs/misc/IF11026.pdf. *See also* Jeremy A. Greene & Kevin R. Riggs, *Why Is There No Generic Insulin? Historical Origins of a Modern Problem*, 372 N. ENG. J. MED. 1171, 1171 (2015). *See also The History of A Wonderful Thing We Call Insulin*, ADA (July 1, 2019), https://www.diabetes.org/blog/history-wonderful-thing-we-call-insulin.

[26] *Diabetes, Symptoms & Causes*, MAYO CLINIC, https://www.mayoclinic.org/diseases-conditions/diabetes/symptoms-causes/syc-20371444 (last viewed Sept. 15, 2020).

[27] *Carbohydrates*, THE AMERICAN HEART ASSOCIATION https://www.heart.org/en/healthy-living/healthy-eating/eat-smart/nutrition-basics/carbohydrates (last reviewed Apr. 16, 2018).

[28] *Id.*

[29] Diabetes Fast Facts, CDC, https://www.cdc.gov/diabetes/basics/quick-facts.html (last viewed Nov. 16, 2020).

[30] *Type 2 Diabetes*, CDC, https://www.cdc.gov/diabetes/basics/type2.html (last reviewed May 30, 2019). *See also The Nutrition Source: Simple Steps to Preventing Diabetes*, HARVARD SCHOOL OF PUBLIC HEALTH, https://www.hsph.harvard.edu/nutritionsource/disease-prevention/diabetes-prevention/ (last viewed Nov. 11, 2020).

[31] *Type 2 Diabetes*, CDC, https://www.cdc.gov/diabetes/basics/type2.html (last reviewed Nov. 16, 2020).

[32] The most common of these medications is metformin, a drug that decreases the amount of sugar the liver makes and increases the body's sensitivity to insulin. Metformin is often the first medication prescribed to Type 2 diabetes patients, and is often combined with other diabetes medications. Metformin was the 4th most commonly prescribed prescription drug in 2019. Sarah Lewis, *The Top 50 Drugs Prescribed in the United States*, HEALTHGRADES (Sept. 5, 2019), https://www.healthgrades.com/right-care/patient-advocate/the-top-50-drugs-prescribed-in-the-united-states.

[33] *Type 1 Diabetes*, CDC, https://www.cdc.gov/diabetes/basics/type1.html (last reviewed Jan. 3, 2021).

and can only be treated with insulin, through multiple daily insulin injections or a continuous insulin pump.[34]

As noted above, Type 1 and Type 2 diabetic patients use a combination of short-acting, rapid-acting, intermediate-acting, and long-acting insulin analogs (e.g., Lantus, Levemir, Toujeo, Tresiba, and Basaglar) to control glucose levels.[35] Today, insulin analogs are widely prescribed by physicians and are the standard of care for people with type 1 diabetes. Insulin can also be one component of care for people with type 2 diabetes, even though insulin analogs are more expensive than other types of insulin.[36]

While type 1 and type 2 diabetes are different in some respects, these diseases share one commonality: significant health risks. If left untreated or under-treated, diabetes can lead to hyperglycemia, cardiovascular disease, kidney disease, blindness, and diabetic ketoacidosis—a build-up of acids in the blood—which may result in a coma or even death.[37] According to the CDC, in 2016, 1.7 million people with diabetes were hospitalized for major cardiovascular disease, such as heart disease or stroke, 188,000 were hospitalized for diabetic ketoacidosis, and 130,000 were hospitalized for lower-extremity amputation.[38] Recently, and as a result of the COVID-19 global pandemic, those with pre-existing conditions, like diabetes, face greater risks of disease complications than the general population.[39] Initial observations also suggest that COVID-19 may be linked to patients developing diabetes or experiencing metabolic complications related to existing diabetes.[40] In addition, diabetes deaths have also been above average in 2020, according to an analysis of estimates from the CDC.[41]

b. How the High Cost of Insulin Negatively Affects Individuals with Diabetes

Approximately 7.4 million Americans use insulin, of which about 1.4 million have type 1 diabetes.[42] However, high-list prices, health plan structures, and high out-of-pocket costs make it

[34] *Id.*
[35] Cigna-SFC-00011177; Cigna-SFC-00011229.
[36] American Diabetes Association, *Pharmacological Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes*, 43 DIABETES CARE 98, 99 (Jan. 2020), https://care.diabetesjournals.org/content/43/Supplement_1/S98.
[37] *Hyperglycemia in diabetes*, MAYO CLINIC, https://www.mayoclinic.org/diseases-conditions/hyperglycemia/symptoms-causes/syc-20373631 (last viewed Nov. 16, 2020); *High blood sugar with type 1 diabetes*, UNIV. OF IOWA STEAD FAMILY CHILDREN'S HOSPITAL, https://www.uichildrens.org/health-library/high-blood-sugar-type-1-diabetes (last viewed Nov. 16, 2020).
[38] CENTERS FOR DISEASE CONTROL AND PREVENTION, NATIONAL DIABETES STATISTICS REPORT (2020), https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf.
[39] *New-Onset Diabetes in COVID-19*, 383 N. ENG. J. MED. 789 (Aug. 2020), https://www.nejm.org/doi/10.1056/NEJMc2018688; Elizabeth Cooney, *Why people with diabetes are being hit so hard by COVID-19*, STAT NEWS (Oct. 1, 2020), https://www.statnews.com/2020/10/01/why-people-with-diabetes-are-being-hit-so-hard-by-covid-19/; Chad Terhune et al., *Why COVID-19 is killing U.S. diabetes patients at alarming rates*, Reuters (July 24, 2020), https://www.reuters.com/article/us-health-coronavirus-diabetes-insight/why-covid-19-is-killing-u-s-diabetes-patients-at-alarming-rates-idUSKCN24P1B4.
[40] *New-Onset Diabetes in COVID-19*, 383 N. ENG. J. MED. 789 (Aug. 2020), https://www.nejm.org/doi/10.1056/NEJMc2018688.
[41] Denise Lu, *2020 Was Especially Deadly. COVID Wasn't the Only Culprit*, N.Y. TIMES (Dec. 13, 2020), https://www.nytimes.com/interactive/2020/12/13/us/deaths-covid-other-causes.html.
[42] American Diabetes Association, *Insulin Access and Affordability Working Group: Conclusions and Recommendations*, 44 DIABETES CARE 1, 2 (Jan. 2020),

more difficult for patients to adhere to their medications, resulting in avoidable complications and higher costs for the U.S. health care system overall.[43] An ADA working group recently noted that "people with high cost-sharing are less adherent to recommended dosing, which results in short- and long-term harm to their health," and further detailed issues that lead to insulin accessibility issues for diabetic patients:

> Formulary exclusions and frequent formulary changes increase financial costs for patients. In addition, patients are bearing more of the cost of medications because of high-deductible plans, increased use of coinsurance, growing number of formulary tiers, and fewer medications covered per tier . . . Since negotiated discounts or rebates are usually not passed directly to people with diabetes, their financial obligations for purchasing insulin are often based on the list price. Clearly, this varies depending on the type of insurance the person has and the type of insulin purchased . . . but specifically impacts those with a high deductible, those who have to pay coinsurance, or those who are in the Medicare Part D coverage gap. People without insurance are often required to pay list price for insulins.[44]

It has been reported that some patients even cross the border into Canada to purchase insulin at lower prices.[45] Some diabetes patients have also resorted to rationing, which can be particularly dangerous to the health of a diabetic and can lead to a variety of complications such as diabetic ketoacidosis—a complication that results in tens of thousands of hospitalizations annually—and can even lead to death.[46] A survey conducted at the Yale Diabetes Center in 2017 found that 1 in 4 people reported rationing their insulin due to financial reasons, contributing to negative health outcomes and poor glycemic control.[47] If this rate of rationing was applied on a national scale, as many as 1.6 million Americans may ration their medication because of cost—highlighting the urgent need to address insulin affordability.

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https://care.diabetesjournals.org/content/early/2018/05/03/dci18-0019. *See also* CENTERS FOR DISEASE CONTROL AND PREVENTION, NATIONAL DIABETES STATISTICS REPORT (2020), https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf.

[43] American Diabetes Association, *Insulin Access and Affordability Working Group: Conclusions and Recommendations*, 44 DIABETES CARE 1, 8 (Jan. 2020), https://care.diabetesjournals.org/content/early/2018/05/03/dci18-0019.

[44] *Id.*

[45] Emily Rauhala, *As the price of insulin soars, American's caravan to Canada for lifesaving medication*, WASH. POST (July 31, 2019), https://www.washingtonpost.com/world/the_americas/as-price-of-insulin-soars-americans-caravan-to-canada-for-lifesaving-medicine/.

[46] American Diabetes Association, *Insulin Access and Affordability Working Group: Conclusions and Recommendations*, 44 DIABETES CARE 1, 8 (Jan. 2020), https://care.diabetesjournals.org/content/early/2018/05/03/dci18-0019. *See also Hyperglycemia in diabetes*, MAYO CLINIC, https://www.mayoclinic.org/diseases-conditions/hyperglycemia/symptoms-causes/syc-20373631 (last viewed Nov. 16, 2020). *See also* Tiffany Stanley, *Life, Death and Insulin, As the costs of lifesaving medication skyrockets, some desperate diabetics are rationing – and risking their lives. Was Alec Raeshawn Smith one of them?*, WASH. POST (Jan. 7, 2019), https://www.washingtonpost.com/news/magazine/wp/2019/01/07/feature/insulin-is-a-lifesaving-drug-but-it-has-become-intolerably-expensive-and-the-consequences-can-be-tragic/?utm_term=.7d6e15666caa&itid=lk_inline_manual_18.

[47] Darby Herkert, et al., *Cost-related Insulin Underuse Among Patients with Diabetes,* JAMA NETWORK (Jan. 2019), https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2717499.

The COVID-19 pandemic has further compounded these problems, as the loss of work and income has made it more difficult for individuals and families to afford their insulin medications.[48] Earlier this year, the ADA conducted a survey of 5,000 people with diabetes nationwide since the start of the pandemic.[49] The ADA found that about 1 in 3 people with diabetes who were employed prior to COVID-19 had lost some or all of their income—rates higher than the general population.[50] The survey also found that, "24% of people with diabetes have used savings, loans or money from stimulus checks to pay for diabetes care in the past three months."[51] A quarter of people with diabetes also reported that they turned to rationing to cut costs whereas others have resorted to underground networks of people who share extra insulin, often free of charge.[52]

While insulin is the focus of the Committee's investigation, it's important to remember that diabetics often have other comorbidities associated with their disease and take other medications to treat conditions such as heart disease, high cholesterol, and hypertension.[53] Often, a large portion of medical costs associated with diabetes is for related comorbidities. For example, in 2017, the ADA estimated that $37 billion in cardiovascular-related spending was associated with diabetes, stating that "the presence of diabetes is associated with greater use of health care services in general." [54] According to the Government Accountability Office (GAO), these services can include "periodic test for blood glucose, eye and foot exams, medical nutrition therapy, and diabetes education . . . [and] services, such as cholesterol tests, smoking cessation tests, smoking cessation services, and influenza immunizations."[55] Taken together, these drugs and preventative measures greatly increase health care costs for diabetic patients in comparison to people who live without the disease.

II. Examining the Flow of Goods and Money in the U.S. Pharmaceutical Supply Chain

The path a drug takes from the manufacturer to the patient is complex and involves multiple financial exchanges. This complexity is caused, in part, by the many different players in the drug supply chain, including drug manufacturers, wholesalers, pharmacies, health insurers, PBMs, employers, and the Federal government.[56] Each link in the supply chain affects the price

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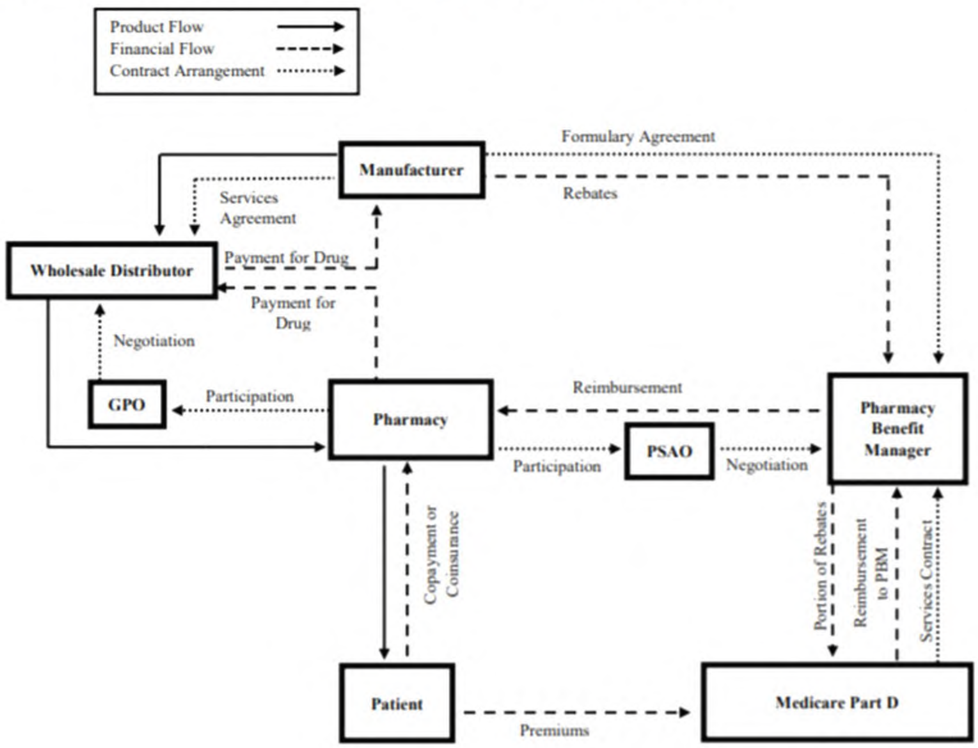
[48] Serena Gordon, *Pandemic Means Financial Hardship for Many with Diabetes*, U.S. NEWS (Aug. 19, 2020), https://www.usnews.com/news/health-news/articles/2020-08-19/pandemic-means-financial-hardship-for-many-with-diabetes.
[49] *Diabetes and COVID-19: New Data Quantifies Extraordinary Challenges Faced by Americans with Diabetes During the Pandemic*, ADA, https://www.diabetes.org/sites/default/files/2020-07/7.29.2020_dQA-ADA%20Data%20Release.pdf.
[50] *Id.*
[51] *Id.*
[52] *Id. See also* Markian Hawryluk, *Not pandemic-proof: Insulin copay caps fall short, fueling underground exchanges*, PITTSBURGH POST-GAZETTE (Oct. 11, 2020), https://www.post-gazette.com/news/insight/2020/10/11/Not-pandemic-proof-Insulin-copay-caps-fall-short-fueling-underground-exchanges/stories/202010110029.
[53] American Diabetes Association, *Economic Costs of Diabetes in the U.S. in 2017*, 41 DIABETES CARE 917, 924 (May 2018), https://care.diabetesjournals.org/content/41/5/917.
[54] *Id.* at 927.
[55] GOV'T ACCOUNTABILITY OFF., MANAGING DIABETES, HEALTH PAN COVERAGE OF SERVICES AND SUPPLIES (Feb. 2005), https://www.gao.gov/new.items/d05210.pdf.
[56] Greg Brown, *The Insulin-Pricing Machine*, BEYOND TYPE 1 (June 18, 2018), https://beyondtype1.org/the-insulin-pricing-machine/.

the patient and payer eventually pays for the drug. This section will briefly explore how drugs are priced and the role of the various players in the drug supply chain.

FIGURE 1: SUPPLY AND PAYMENT CHAIN FOR PART D-COVERED DRUGS (NON-SPECIALTY)



Adapted from: Adam J. Fein, Follow the Dollar Math: How Much Do Pharmacies, Wholesalers, and PBMs Make From a Prescription? (Aug 8, 2017), https://www.drugchannels.net/2017/08/follow-dollar-math-how-much-do.html.

a. Drug Manufacturers

There are two types of drug manufacturers—those that manufacture brand-name drugs and those that manufacture generic drugs.[57] While brand-name and generic manufacturers share similarities, "the branded drug business model requires very heavy investments in R&D and marketing [whereas] … the generic drug model requires particularly strong competence in manufacturing, channel management and patent litigation."[58] This report focuses on three brand-name insulin manufacturers: Sanofi, Novo Nordisk, and Eli Lilly. Therefore, it will not discuss generic manufacturers in depth. However, it's important to distinguish between these two business models because it affects the price manufacturers initially set for their product, known as the wholesale acquisition cost (WAC), which is colloquially known as the "list price."

Drug manufacturers are solely responsible for determining the WAC of their products. Internal documents produced to the Committee show that companies set their WAC price for insulin based on competitive considerations in the insulin market, maximizing revenue, and

[57] Samuel H. Kina and Marta Wosinska, *Pharmaceutical pricing*, IN HANDBOOK OF PRICING RESEARCH AND MARKETING 488, 490 (2009).
[58] *Id.*

maximizing market share. In response to the Committee, Sanofi asserted that R&D, marketing, and patent status factor into WAC.[59] However, documents produced to the Committee did not fully support the company's assertion. In fact, it appears that the only instance in which R&D costs appear to have been considered by one of the three manufacturers in relation to WAC price or rebate offers was when an Eli Lilly executive asked subordinates whether a requested bid from the Department of Veterans Affairs would result in too much of the company's manufacturing capacity being used for business that generated low margins.[60]

i. Research & Development, Sales & Marketing

1. Eli Lilly

During this investigation, the Committee requested that Sanofi, Novo Nordisk, and Eli Lilly "provide an itemized accounting of [insulin] R&D costs that breaks out costs by activity (e.g., basic research, clinical trials for marketing approval, post-marketing research and surveillance, etc.)" and "how each activity directly supports R&D for insulin products."[61] In response, Eli Lilly estimated that:

> [B]etween 2014 and 2018, it has spent approximately $244 million on research and development related to Humalog globally, $66 million on research and development related to Humulin globally, and $85 million on research and development related to Basaglar globally."[62]

However, this spending represents a fraction of the $22.4 billion in revenue Eli Lilly reported for these therapies during the same five-year period—$14.3 billion for Humalog, $6.8 billion for Humulin, and $1.3 billion for Basaglar.[63]

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[59] Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, on Behalf of Sanofi, to Senator Grassley and Senator Wyden (Mar. 29, 2019).

[60] LLY-SFCOM-UR-00003543, at LLY-SFC-UR-00003543-44.

[61] Letter from Senator Grassley and Senator Wyden to Lars Fruergaard Jorgensen, President and Chief Executive Officer, Novo Nordisk (Feb. 22, 2019).

[62] Letter from Reginald Brown, Counsel, WilmerHale, on Behalf of Eli Lilly, to Senator Grassley and Senator Wyden (Mar. 8, 2019).

[63] Revenue derived from Forms 10-K that Eli Lilly filed with the Securities and Exchange Commission for years 2014-2018. According to Eli Lilly, the company does not maintain net revenue at the NDC level on a consistent and audited basis. The company therefore produced gross revenue at the NDC level and net revenue at the consolidated product family level. *See* Letter from Reginald Brown, Counsel, WilmerHale, on Behalf of Eli Lilly, to Senator Grassley and Senator Wyden (Mar. 8, 2019). *See also* LLY-SFCOM-00000002. *Eli Lilly 10-k (2018)*, SEC, https://www.sec.gov/Archives/edgar/data/59478/000005947819000082/lly-20181231x10xk.htm; *Eli Lilly 10-k (2016)*, SEC, https://www.sec.gov/Archives/edgar/data/59478/000005947817000098/lly-20161231x10xk.htm.

Net Sales of Eli Lilly Insulin Products in Millions of Dollars (2014-2018)						
	2014	**2015**	**2016**	**2017**	**2018**	**Total**
Humalog	$2,785.2	$2,841.9	$2,768.8	$2,865.2	$2,996.5	**$14,257.6**
Humulin	$1,400.1	$1,348.3	$1,365.9	$1,335.4	$1,331.4	**$6,781.1**
Basaglar	--	$11.1	$86.1	$432.1	$801.2	**$1,330.5**
Total	**$4,185.3**	**$4,201.3**	**$4,220.8**	**$4,632.7**	**$5,129.1**	**$22,369.2**
Source: Eli Lilly Form 10-K, Securities and Exchange Commission						

Eli Lilly further explained that it could not provide a full breakdown of its R&D spending because "certain costs, such as local medical expenses and billable hours for training and administrative activities are not allocated by product."[64] R&D spending also represents a fraction of the money Eli Lilly spent on marketing the drugs. Eli Lilly reported spending nearly $1.5 billion on sales and marketing expenses on the drugs, which the company cautioned may not capture all such expenses.[65]

[64] Letter from Reginald Brown, Counsel, WilmerHale, on Behalf of Eli Lilly, to Senator Grassley and Senator Wyden (Mar. 8, 2019).

[65] LLY-SFCOM-00000045. Eli Lilly noted that "Marketing and Advertising expenses not tracked at SKU level (Pen, vial, Mixes, etc.) . . . For purposes of this report, all expenses shown at a consolidated 'Total Insulins' level . . . Certain marketing and advertising expenses incurred at Diabetes portfolio level (i.e., Requiring an allocation to the brands) are not included in this report." *Id.*

Sales Expenses for Eli Lilly Insulins (Humalog, Humulin, Basaglar), 2014-2018						
	2014	**2015**	**2016**	**2017**	**2018**	**Total**
Sales Force[1]	$136,086,445	$94,518,702	$83,835,211	$79,667,141	$87,511,840	**$481,619,340**
Market Research[2]	$8,672,584	$7,638,121	$7,147,827	$3,584,742	$2,799,660	**$29,842,934**
Samples[3]	$17,814,969	$12,817,014	$9,776,947	$8,399,706	$11,313,803	**$60,122,440**
3rd Party Vendors[4]	$61,909,679	$54,371,417	$89,351,175	$94,728,535	$82,725,285	**$383,086,091**
Medical Conference Sponsorships[5]	$227,961	$155,092	$47,512	$187,850	$37,172	**$655,587**
Other[6]	$4,874,300	$7,154,787	$6,645,130	$2,864,632	$2,514,864	**$24,053,713**
Total	**$229,585,940**	**$176,655,133**	**$196,803,802**	**$189,432,606**	**$186,902,624**	**$979,380,105**

Source: LLY-SFCOM-00000045; LLY-SFCOM-00002499.

[1] *Compensation and Benefits of Lilly Sales force for Humalog, Humulin, Basaglar. Includes meal, travel, meetings, etc.*

[2] *Includes IMS Health secondary (physician prescribing) data purchases, analytics charges.*

[3] *Includes cost of sample only, no distribution/packing costs.*

[4] *Digital Media, agency fees, patient support programs, etc.*

[5] *Exhibition fees for congress/conferences.*

[6] *Includes Compensation and Benefits of Lilly Marketing team.*

Marketing Expenses for Eli Lilly Insulins (Humalog, Humulin, Basaglar), 2014-2018						
	2014	**2015**	**2016**	**2017**	**2018**	**Total**
Consumer Marketing[1]	$22,286,002	$15,931,892	$21,679,235	$22,686,366	$23,371,480	**$105,954,975**
Prescriber Marketing[2]	$22,779,532	$15,279,295	$36,251,278	$44,687,503	$34,404,984	**$153,402,592**
Other[3]	$47,838,126	$49,391,585	$54,498,308	$38,566,312	$25,914,074	**$216,208,405**
Patient Support[4]	$595,834	$1,533,658	$539,770	$3,825,284	$15,700,246	**$22,194,793**
Total	**$93,499,494**	**$82,136,431**	**$112,968,591**	**$109,765,465**	**$99,390,784**	**$497,760,765**

Source: LLY-SFCOM-00002499.

[1] *Consumer expenses reflect promotional activities designed to support patients initiating insulin treatment whom already received an insulin prescription from their Health Care Provider. Examples include branded paid search advertising and printed materials for patients. Also, included are unbranded disease state education digital content sponsored by LillyUSA, LLC. This may also include branded advertising presented alongside unbranded content. These expenses, including the unbranded content, are classified as promotional advertising by Eli Lilly & Co.*

[2] *Prescriber expenses reflect marketing programs designed to educate health care professionals prescribing insulin about Lilly products. These expenses include peer to peer programs (physicians educating other physicians) and Lilly's presence at medical conferences. Prescriber expenses do not include any costs for Lilly Sales force.*

[3] *Samples, Market Research, Analytics, Payer, Cover My Meds.*

[4] *Patient Support expenses reflect the operating expenses to administer insulin affordability programs. Expenses in this line do not include actual dollars spent on copay assistance (as such figures are accounted for as Gross to Net Sales adjustments in accordance with Generally Accepted Accounting Principles).*

According to internal memoranda prepared for Eli Lilly's executive committee, in November 2016, the company assumed its "core insulins" would earn revenue of $3.3 billion in 2017 ($4 billion worldwide).[66] In order to achieve these results, Eli Lilly sought to improve its competitive position with respect to its key brands and planned to devote a majority of its R&D spending on clinical trials for existing Type 2 diabetes drugs—Jardiance,[67] Tranjenta,[68] and Trulicity[69]—the last of which was Eli Lilly's "largest growth driver."[70] Indeed, according to Eli Lilly, "Trulicity has been a catalyst . . . with growth driven by investments in [direct to consumer], sales force reach, and access."[71] These post-marketing clinical trials were intended to show that the therapy helped reduce incidence of cardiovascular disease which allowed Eli Lilly to seek an expansion of its FDA label indication.[72] However, even with these significant studies, the company's R&D spending for its entire diabetes franchise was budgeted to be just one-third of its sales, goods and administrative expenses, and, in fact, less than the cost of a single line item—Eli Lilly's global diabetes salesforce.[73] The following table details Eli Lilly's funded initiatives and sales force spending between 2017 and 2018.[74]

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[66] LLY-SFCOM-UR-00006920; LLY-SFCOM-UR-00006921; LLY-SFCOM-UR-00006924, at LLY-SFCOM-UR-00006925.

[67] Press Release, Eli Lilly, Jardiance meets primary endpoint in reducing risk of cardiovascular death or hospitalization for heart failure in phase III clinical trial in adults with and without diabetes (July 2020), https://investor.lilly.com/news-releases/news-release-details/jardiancer-meets-primary-endpoint-reducing-risk-cardiovascular.

[68] Press Release, Eli Lilly, Boehringer Ingelheim and Lilly full results of Tradjenta's CARMELINA cardiovascular outcome trial (Oct. 4, 2018), https://investor.lilly.com/news-releases/news-release-details/boehringer-ingelheim-and-lilly-present-full-results-tradjentars.

[69] Press Release, Eli Lilly, Trulicity significantly reduced major cardiovascular events for broad range of people with type 2 diabetes (Jul. 9, 2019), https://investor.lilly.com/news-releases/news-release-details/trulicityr-dulaglutide-significantly-reduced-major.

[70] LLY-SFCOM-UR-00006924, at LLY-SFCOM-UR-00006952.

[71] LLY-SFCOM-UR-00006921, at LLY-SFCOM-UR-00006922. Trulicity, Jaridance and Trajenta are marketed and manufactured in partnership with Boehringer Ingelheim.

[72] For example, in February 2020, Eli Lilly announced that the FDA approved Trulicity for the reduction of major adverse cardiovascular events in adults with type 2 diabetes. According to Eli Lilly, this new indication makes Trulicity the only type 2 medicine approved to reduce these risks. *See* Press Release, Eli Lilly, Trulicity is the first and only type 2 diabetes medicine approved to reduce cardiovascular events in adults with and without established cardiovascular disease (Feb. 21, 2020), https://investor.lilly.com/news-releases/news-release-details/trulicityr-dulaglutide-first-and-only-type-2-diabetes-medicine. LLY-SFCOM-UR-00006921; LLY-SFCOM-UR-00006924, at LLY-SFCOM-UR-00006952.

[73] LLY-SFCOM-00000045; LLY-SFCOM-00002499; LLY-SFCOM-UR-00006921; LLY-SFCOM-UR-00006924, at LLY-SFCOM-UR-00006952.

[74] LLY-SFCOM-UR-00006924, at LLY-SFCOM-UR-00006952.

Funded Initiatives

SG&A			
Funded Priorities - Total Spend for Each Item/Initiative included in Add-up while achieving Target			
		Priority Level	
2017	2018	A/B/C	
294	298	A	Competitive investment in Trulicity to deliver ~$1bn in YOY BAC growth; includes DTC [2017: $140m and 2018: $142m]
118	113	A	Prepare to capitalize on Jardiance CV label outcome
97	100	A	Retain and protect the $3.3bn insulin franchise [DBU markets]
22	22	A	Capitalize on Humulin U500 KwikPen launch uptake
22	32	A	Pre-launch investment in Nasal Glucagon and Connected Care [US and Global]
116	116	A	Regional / Global initiatives - marketing, communications, strategy, operations, market research, admin, evolution
712	738	A	Diabetes Salesforce [2017 values - US: $423m; EUCAN: $180m; Japan: $109m]
49	49	B	Optimize Basaglar investment
41	42	B	Non-Branded HCP, Consumer and Payer Initiatives
28	27	C	Trajenta SG&A - aligned investment with BI [23% SG&A/Sales delivering ~$400m in Revenue (LLY share)]
[redacted]			
55	41		Pharma Fee all products - Fixed
1584	1609		SG&A Total

R&D			
Funded Priorities - Total Spend for Each Item/Initiative included in Add-up while achieving Target			
		Priority Level	
2017	2018	A/B/C	
140	118	A	Trulicity REWIND extension, high dose Ph2 study, and Pediatric study
89	61	A	Jardiance heart failure, Japan safety and efficacy studies, Type 1 DM, post-marketing
88	87	A	Global Medical
59	54	A	Trajenta CVOT (CAROLINA and CARMELINA), pediatric, add-on to basal
43	32	A	Insulins; partnership with Insulet; device updates; Humulin U500
22	43	A	Nasal Glucagon; includes milestone in 2018
122	152	B	Corp Development Multi-Molecule/Non-Molecule
10	8	B	Basaglar U200 and China
4	0	B	DNR-free vial stoppers - Humalog and Humulin
3	8	C	Other Development initiatives
3	0	C	PCSK9 Phase 3 enabling
-41	-40	C	Admin Objective
542	522		R&D Total

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2. Sanofi

In response to the Committee's request, Sanofi estimated that it had invested approximately $4.5 billion in diabetes, which includes both insulin and non-insulin products, between 2012 and 2018, noting that it spent $800 million in 2018 on diabetes alone.[75] Sanofi only provided R&D product-specific data for 2014 to 2018, and limited the data to five insulin products.[76] Therefore, the Committee was unable to confirm Sanofi's total R&D spending on its diabetes franchises. However, R&D spending (which was reported to the Committee in dollars) on these five diabetes products accounted for a fraction of the company's reported revenue from its diabetes franchise, as reported to the U.S. Securities and Exchange Commission.[77] From 2014 to 2018, the company's diabetes franchise generated nearly €31 billion in net sales

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[75] Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, on Behalf of Sanofi, to Senator Grassley and Senator Wyden (Mar. 8, 2019).
[76] Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, on Behalf of Sanofi, to Senator Grassley and Senator Wyden (Mar. 29, 2019).
[77] *Id.* Sanofi produced data regarding gross sales, net sales, and gross units by product line, which is how Sanofi tracks this information. *Id.*

(approximately $37 billion based on current currency conversion rates), [78] whereas R&D spending for these five insulin products was approximately $902 million.[79]

Net Sales of Sanofi Diabetes Products in Millions of Euros (2014-2018)

	2014	2015	2016	2017	2018	Total
Admelog					€ 93	**€ 93**
Apidra	€ 336	€ 376	€ 367	€ 286	€ 357	**€ 1,722**
Lantus	€ 6,344	€ 6,390	€ 5,714	€ 4,761	€ 3,565	**€ 26,774**
Soliqua					€ 73	**€ 73**
Toujeo		€ 164	€ 649	€ 630	€ 840	**€ 2,283**
Total	**€ 6,680**	**€ 6,930**	**€ 6,730**	**€ 5,677**	**€ 4,928**	**€ 30,945**

Source: Securities and Exchange Commission. According to Sanofi, "[n]et sales comprise revenue from sales of pharmaceutical products, consumer healthcare products, active ingredients and vaccines, net of sales returns, of customer incentives and discounts, and of certain sales-based payments paid or payable to the healthcare authorities." (Sanofi, 20-F, 2019)

Sanofi R&D Spending by Product in Millions of Dollars (2014-2018)

	2014	2015	2016	2017	2018	Total
Admelog	$ 24.45	$ 54.53	$ 38.25	$ 11.26	$ 6.15	**$ 134.64**
Apidra	$ 2.31	$ 5.47	$ 3.64	$ 1.36	$ 1.04	**$ 13.82**
Lantus	$ 42.79	$ 21.95	$ 20.76	$ 16.44	$ 8.24	**$ 110.18**
Soliqua	$ -	$ 1.03	$ 40.94	$ 70.76	$ 68.74	**$ 181.47**
Toujeo	$ 67.53	$ 72.45	$ 150.25	$ 117.84	$ 54.43	**$ 462.50**
Total	**$ 137.08**	**$ 155.43**	**$ 253.84**	**$ 217.66**	**$ 138.60**	**$ 902.61**

Source: Letter to Senator Grassley and Senator Wyden from Jeffrey Handwerker, Counsel, Sanofi (March 29, 2019).

3. Novo Nordisk

Novo Nordisk failed to provide a detailed accounting of its R&D expenditures to the Committee. However, on its annual report submitted to the SEC, the company reported that it spent approximately 36 million Danish krone related to diabetes and obesity R&D between 2017 and 2019.[80]

b. Wholesale Distributors and Pharmacies

Drugs are purchased directly by wholesale distributors and delivered to a variety of customers, including pharmacies, physicians, hospitals, and other medical facilities. Wholesale distributors negotiate with drug manufacturers for discounts off a drug's list price, often referred

[78] Sanofi reported net sales in Euros to the Securities and Exchange Commission.
[79] *Id.*
[80] *See Novo Nordisk Annual Report 2019*, NOVO NORDISK at 52 (2019), https://www.novonordisk.com/content/dam/nncorp/global/en/annual-report/pdfs/2019/Novo-Nordisk-Annual-Report-2019.pdf.

to as the wholesale acquisition cost (WAC).[81] Examples of discounts include volume discounts, inventory claw backs, and prompt pay discounts. The wholesale distributor then sells the product to a pharmacy, hospital, or other medical facility at WAC plus some negotiated percentage.[82]

The outcome of these negotiations is critical to a drug's success because wholesale distributors help connect pharmacies, hospitals, and other medical facilities to drug manufacturers. However, over the past 30 years, the wholesale distribution industry has become highly consolidated. In 2018, the three largest wholesale distributors—AmerisourceBergen, McKesson, and Cardinal Health—covered 95% of the market.[83] This consolidation allows wholesale distributors to use aggressive disruption techniques to secure favorable agreements, such as the refusal to stock new product, reduce service levels on certain drugs, or ordering the slowdown of drug distribution in non-U.S. countries.[84]

At the pharmacy level, payers and PBMs reimburse pharmacies for the drugs they disburse to patients. However, payments vary.[85] For example, contracts typically set pharmacy reimbursement as the lesser of (1) the over-the-counter cash price, (2) the drug cost plus a dispensing fee, (3) the contractual rate, or (4) if a generic drug, the Maximum Allowable Cost (MAC) on a MAC list.[86] Insulin drugs are not included on MAC lists because it is regulated as a biologic and has no generic alternatives.

c. Health Insurance

In the United States today, a majority of Americans receive coverage through a private health insurer. Most of these Americans—about 158 million people, or 49% of the country—receive coverage through an employer, while a smaller portion—nearly 19 million people—receive private coverage directly from an insurer, including through the Affordable Care Act's (ACA) marketplaces.[87] The remaining insured population is generally divided between Medicaid and Medicare, which covered approximately 20% and 14% of the country, respectively, in 2019.[88] That same year, nearly 29 million nonelderly Americans were uninsured.[89] Notably, the COVID-19 pandemic has altered this coverage landscape as job losses and lost income led many Americans to seek coverage through Medicaid and the marketplace.[90] For the purposes of this

[81] Samuel H. Kina and Marta Wosinska, *Pharmaceutical pricing*, IN HANDBOOK OF PRICING RESEARCH AND MARKETING 488, 500 (2009).
[82] *Id.* at 500-01.
[83] Adam Fein, *The Big Three Wholesalers: Revenues and Channel Share Up, Profits Down*, DRUG CHANNELS (Oct. 2, 2019), https://www.drugchannels.net/2019/10/the-big-three-wholesalers-revenues-and.html.
[84] SANOFI_SFC_00013920.
[85] Samuel H. Kina and Marta Wosinska, *Pharmaceutical pricing*, IN HANDBOOK OF PRICING RESEARCH AND MARKETING 488, 502 (2009).
[86] ORX_Sen_Fin_0009800. *See also* Samuel H. Kina and Marta Wosinska, *Pharmaceutical pricing*, IN HANDBOOK OF PRICING RESEARCH AND MARKETING 488, 502 (2009).
[87] *Health Insurance Coverage of Total Population*, KFF https://www.kff.org/other/state-indicator/total-population/ (last viewed July 7, 2020).
[88] *Id.*
[89] Jennifer Tolbert and Kendal Orgera, *Key Facts About the Uninsured Population*, KFF (Nov. 6, 2020), https://www.kff.org/uninsured/issue-brief/key-facts-about-the-uninsured-population/.
[90] M. Karpman and S. Zuckerman, *ACA Offers Protection as the COVID-19 Pandemic Erodes Employer Health Insurance Coverage*, URBAN INSTITUTE (Nov. 6, 2020), https://www.rwjf.org/en/library/research/2020/11/aca-offers-protection-as-the-covid-19-pandemic-erodes-employer-health-insurance-coverage.html.

discussion, we will provide a brief overview of how Medicare, Medicaid, and employer-sponsored insurance generally pays for insulin products.

i. Medicare Part D

Medicare provides optional prescription drug coverage through its Part D benefit, which is provided through private plans that are approved by the Federal government.[91] Beneficiaries can choose Medicare Part D stand-alone prescription drug plans (PDPs) or enroll in Medicare Advantage (MA-PD) plans that offer drug coverage in addition to all other Medicare benefits.[92] In 2020, over 75% of Medicare beneficiaries were enrolled in Part D plans.[93] PDPs and MA-PD plans must offer enrollees the *standard drug benefit* or alternative coverage that is the *actuarially equivalent* in value. Part D plan formularies must include a minimum of two chemically distinct drugs in each drug class and are required to cover all drugs in the six protected classes: immunosuppressants, antidepressants, antipsychotics, anticonvulsants, antiretrovirals, and antineoplastics.[94]

The Part D standard drug benefit provides different levels of coverage and cost-sharing at different phases of the benefit. These phases include a deductible, an initial coverage phase, a coverage gap, and catastrophic coverage.[95] For 2020, the standard drug benefit included a $435 deductible and a 25% coinsurance until the enrollee and plan reached $4,020 in total drug spending.[96] After this point, the enrollee enters the coverage gap phase (also referred to as the *doughnut hole*) and continues to pay a 25% coinsurance for both brand-name and generic drugs. For brand-name drugs, manufacturers pay a 70% discount on the drug while the plan pays 5%.[97] Whereas, for generic drugs, the plan pays 75%.[98] Once the enrollee's out-of-pocket costs exceeded $6,350 (an estimated $9,719 in total spending by the plan and enrollee), they reach what is known as the catastrophic phase of the Medicare Part D benefit. In this phase, Medicare pays 80%, plans pay 15%, and the enrollee must pay the greater of 5% in coinsurance or $3.60 for a generic drug and $8.95 for a brand-name drug.[99] Updated coverage parameters for 2021 are reflected in the figure below.[100]

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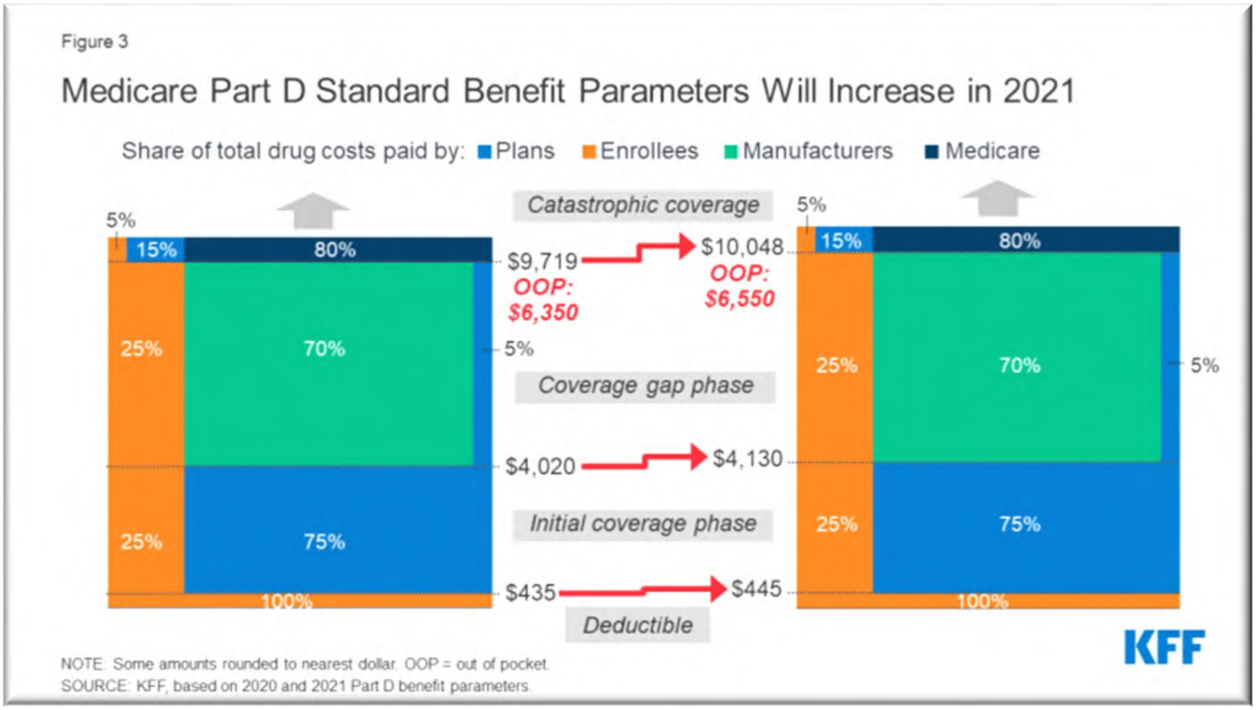
[91] CONG. RES. SERV., MEDICARE PRIMER, at 23 (May 21, 2020), https://fas.org/sgp/crs/misc/R40425.pdf.
[92] *An Overview of the Medicare Part D Prescription Drug Benefit,* KFF (Oct. 14, 2020), https://www.kff.org/medicare/fact-sheet/an-overview-of-the-medicare-part-d-prescription-drug-benefit/.
[93] *Id.*
[94] *Id.*
[95] *Id.*
[96] CONG. RES. SERV., MEDICARE PRIMER, at 23 (May 21, 2020), https://fas.org/sgp/crs/misc/R40425.pdf.
[97] *Id.* at 23-24.
[98] *Id.*
[99] *Id.* at 24. *See An Overview of the Medicare Part D Prescription Drug Benefit*, KFF (Oct. 14, 2020), https://www.kff.org/medicare/fact-sheet/an-overview-of-the-medicare-part-d-prescription-drug-benefit/.
[100] *An Overview of the Medicare Part D Prescription Drug Benefit*, KFF (Oct. 14, 2020), https://www.kff.org/medicare/fact-sheet/an-overview-of-the-medicare-part-d-prescription-drug-benefit/.



In addition to paying nearly all drug costs above the catastrophic threshold of the standard drug benefit (*reinsurance*), Medicare also pays plans monthly *direct subsidies* to Part D plans for each enrollee. Every year, Part D plan sponsors submit bids to CMS estimating the cost to provide drug coverage to beneficiaries. The Federal government then pays Part D sponsors a risk-adjusted amount based on the nationwide average of all plan bids (*direct subsidies*).[101] In addition, Medicare also pays Part D plan sponsors an additional subsidy for providing drug benefits to low-income beneficiaries. For example, if a beneficiary is dual-eligible (meaning they qualify for both Medicare and Medicaid) or if they meet certain income benchmarks, Medicare pays additional subsidies to help cover the beneficiary's out-of-pocket costs, including premiums, deductibles, and lowered cost-sharing for prescriptions.[102] Dual-eligible beneficiaries and certain other low-income beneficiaries are also automatically enrolled in a PDP if they do not choose a plan on their own.[103]

According to the Congressional Budget Office (CBO), Medicare Part D spending will total $96 billion in 2021, or approximately 13% of total Medicare spending.[104] CBO further estimates that Part D spending will total $192 billion by 2030.[105] This dramatic rise in spending is due in part to the availability of more expensive drugs—many of which cost more than $7,500

[101] *Part D Payment System,* MedPAC (Oct. 2016), http://www.medpac.gov/docs/default-source/payment-basics/medpac_payment_basics_16_partd_final.pdf?sfvrsn=0.
[102] CONG. RES. SERV., MEDICARE PRIMER, at 25 (May 21, 2020), https://fas.org/sgp/crs/misc/R40425.pdf
[103] *An Overview of the Medicare Part D Prescription Drug Benefit*, KFF (Oct. 14, 2020), https://www.kff.org/medicare/fact-sheet/an-overview-of-the-medicare-part-d-prescription-drug-benefit/.
[104] *Id.*
[105] CONG. BUDGET. OFF., MEDICARE—CBO'S MAY 2020 BASELINE (Mar. 2020), https://www.cbo.gov/system/files/2020-03/51302-2020-03-medicare.pdf.

annually—causing the Federal government to pay higher reinsurance subsidies to plans.[106] Additionally, for Medicare beneficiaries, there is no cap on individual out-of-pocket spending, so individual costs can be quite high.[107] High costs can be especially problematic for people with diabetes who tend to have comorbidities, such as hypertension, obesity, or hyperlipidemia (or excess fat in the blood), and must use several drugs to stay healthy.[108]

ii. Medicaid Drug Rebate Program

Medicaid is a joint Federal-state program that provides health insurance coverage for low-income individuals and families. Though states are not required to cover prescription drugs, all state Medicaid programs currently provide this benefit.[109] Medicaid spending for prescription drugs is largely shaped by the Medicaid Drug Rebate Program (MDRP), which requires drug manufacturers to enter into rebate agreements with the Federal government in exchange for having nearly all of their drugs covered by the Medicaid program. Under the MDRP, for each drug administered to a Medicaid beneficiary, a manufacturer must provide a rebate to the state, which shares a portion of the drug rebate with the Federal government.[110] The formula for these rebates is set by statute and differs for generic and brand name drugs. For generic drugs, the rebate is 13% of the Average Manufacturer Price (AMP), which is the average price paid to drug manufacturers by wholesalers and pharmacies.[111] For brand name drugs, manufacturers pay 23.1% of the AMP or the difference between AMP and the "best price," whichever is greater.[112] The "best price" is defined as the lowest price at which the manufacturer sold a drug to any wholesaler, retailer, provider, or other entity within or outside of Medicaid, excluding certain government programs.[113] In this way, the best price requirement ensures that Medicaid receives the lowest price available *to any purchaser in any state* for a brand name drug.[114]

The MDRP plays a key role in reducing Federal and state spending on prescription drugs. In 2017, Medicaid spent approximately $64 billion on prescription drugs and collected more than half of that in rebates (nearly $35 billion), reducing net spending to just over $29 billion.[115] However, the MDRP also places some limits on states' ability to negotiate lower prices directly with manufacturers, which can increase Medicaid's exposure to new high-cost blockbuster drugs. For example, in the case of Sovaldi, Medicaid programs found themselves unable to extract additional, supplemental rebates from Gilead Sciences until the company was forced to offer more generous rebates in response to market competition in the therapeutic class. The high

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[106] Mike McCaughan, *Medicare Part D*, HEALTH AFFAIRS (Aug. 10, 2017), https://www.healthaffairs.org/do/10.1377/hpb20171008.000172/full/.
[107] *Id.*
[108] Helena Rodboard, et al., *Impact of type 2 diabetes mellitus on prescription medication burden and out-of-pocket healthcare expenses*, DIABETES RES. CLIN. PRACT. (Mar. 2010), https://pubmed.ncbi.nlm.nih.gov/20047768/.
[109] *Prescription Drugs*, MEDICAID.GOV, https://www.medicaid.gov/medicaid/prescription-drugs/index.html (last viewed Dec. 29, 2020).
[110] *Understanding the Medicaid Prescription Drug Rebate Program,* KFF (Nov. 12, 2019), https://www.kff.org/medicaid/issue-brief/understanding-the-medicaid-prescription-drug-rebate-program/.
[111] *Id.*
[112] *Id.*
[113] 42 U.S.C. § 1396r-8(c)(1)(C)(i).
[114] *Medicaid Payment for Outpatient Prescription Drugs*, MACPAC (May 2018), https://www.macpac.gov/wp-content/uploads/2015/09/Medicaid-Payment-for-Outpatient-Prescription-Drugs.pdf.
[115] *Medicaid Drug Spending Trends*, MACPAC (Feb. 2019), https://www.macpac.gov/wp-content/uploads/2019/02/Medicaid-Drug-Spending-Trends.pdf.

cost of Sovaldi initially led some states to restrict access to the drug to the sickest patients, reducing access to program beneficiaries.[116] Furthermore, as will be discussed below, the MDRP may influence drug spending outside of Medicaid by leading some drug manufacturers to inflate their launch prices and avoid setting new and lower "best prices" for their products.[117]

iii. Employer-sponsored health insurance

Collectively, employers are another major payer of prescription drugs. Employer-sponsored health insurance is health coverage offered by employers to employees, and sometimes their dependents, as a benefit of employment. Nearly all covered workers have prescription drug coverage through their plans.[118] However, many enrollees can still face significant cost-sharing in the form of high deductibles or coinsurance.[119] Approximately 30% of adults with employer-sponsored plans are enrolled in high-deductible-health-plans (HDHP).[120] In 2021, HDHPs (as defined by the Internal Revenue Service) require a deductible of at least $1,400 for an individual and $2,800 for a family.[121] HDHPs are often touted as a way to mitigate rising premiums, but for individuals with lifelong illnesses like diabetes, the financial exposure fundamental to HDHPs may contribute to their decision to delay medical treatment.

For example, several studies have found that diabetics who enroll in HDHPs often do not refill branded medications or delay treatment altogether, contributing to problems with adherence.[122] Delaying treatment can be disastrous to one's health or even deadly, and from an economic perspective, delayed treatment leads to increased health care costs for patients and payers in the long-term. The Internal Revenue Service sought to address this issue in July 2019 when it released guidance that expanded the list of preventative services that a HDHP can cover below the deductible to include insulin.[123]

d. The PBM Industry

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[116] *See* Press release, Wyden-Grassley Solvaldi Investigation Finds Revenue-Driven Pricing Strategy Behind $84,000 Hepatitis Drug (Dec. 2015), https://www.finance.senate.gov/ranking-members-news/wyden-grassley-sovaldi-investigation-finds-revenue-driven-pricing-strategy-behind-84-000-hepatitis-drug.
[117] Rachel Dolan, *Understanding the Medicaid Prescription Drug Rebate Program*, KFF (Nov. 12, 2019), https://www.kff.org/medicaid/issue-brief/understanding-the-medicaid-prescription-drug-rebate-program/.
[118]Adam Fein, *Employer Pharmacy Benefits in 2019: High Deductibles and Greater Coinsurance Expose Even More Patients to Prescription List Prices*, DRUG CHANNELS (Nov. 13, 2019), https://www.drugchannels.net/2019/11/employer-pharmacy-benefits-in-2019-high.html.
[119] *Id.*
[120] *2019 Employer Health Benefits Survey*, KFF (Sept. 25, 2019), https://www.kff.org/report-section/ehbs-2019-section-8-high-deductible-health-plans-with-savings-option/#figure85.
[121] INTERNAL REVENUE PROCEDURE 2020-32, https://www.irs.gov/pub/irs-drop/rp-20-32.pdf (Total out-of-pocket expenses for the year are capped at $7,000 for individuals and $14,000 for families). *See also* A. Mark Fendrick et al., *Association between Switching to a high-deductible health plan and discontinuation of Type 2 diabetes treatment*, JAMA Network (Nov. 1, 2019), https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2753788.
[122] A. Mark Fendrick et al., *Association between Switching to a high-deductible health plan and discontinuation of Type 2 diabetes treatment*, JAMA Network (Nov. 1, 2019), https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2753788; J. Frank Wharam, *et al.*, *High-Deductible Insurance and Delay in Care for the Microvascular Complications of Diabetes*, ANNALS OF INTERNAL MEDICINE (Dec. 18, 2018), https://www.acpjournals.org/doi/10.7326/M17-3365.
[123] Press release, IRS expands list of preventive care for HSA participants to include certain care for chronic conditions (July 17, 2019), https://www.irs.gov/newsroom/irs-expands-list-of-preventive-care-for-hsa-participants-to-include-certain-care-for-chronic-conditions.

PBMs administer prescription drug benefits on behalf of health insurers and payers, including employers, state Medicaid agencies, and commercial insurers that provide employer-sponsored insurance and coverage through Medicare, Medicaid, or CHIP.[124] The largest PBMs administer drug benefits for health plans that insure tens of millions of people (often referred to as "covered lives"), giving these PBMs tremendous bargaining power in negotiations with pharmaceutical manufacturers seeking access to, and favorable placement on, health insurers' formularies. PBMs use this power to negotiate with drug manufacturers, ostensibly to lower drug costs for their clients.

Manufacturers have a strong financial incentive to gain access to a plan sponsor's formulary, particularly national formularies administered by the three largest PBMs on behalf of hundreds or thousands of health plan clients. PBMs also negotiate formularies on behalf of individual clients. As Eli Lilly explained to its investors in 2019, failing to secure formulary placement can "lead to reduced usage of a drug for the relevant patient population due to coverage restrictions, such as prior authorizations and formulary exclusions, or due to reimbursement limitations which result in higher consumer out-of-pocket cost, such as non-preferred co-pay tiers, increased co-insurance levels, and higher deductibles."[125] This is why pharmaceutical manufacturers compete fiercely for formulary placement, particularly in therapeutic areas such as diabetes where there are multiple branded products with similar clinical attributes. They also seek to balance drug price increases and price concessions—primarily rebates and price protection clauses—to compete against each other for favorable formulary placement with health plans represented by PBMs and health plans that choose to negotiate with manufacturers directly.[126]

The PBM industry has grown and consolidated rapidly in recent decades. As an example, in 1989, roughly 60 million people had their prescription drug coverage administered by PBMs.[127] A few years later, just five companies controlled roughly 80% of a 100 million person market[128] and, by 2014, health care experts estimated three companies—CVS Caremark, Express Scripts, and OptumRx—served over 180 million people, representing roughly 80% of people whose pharmacy benefits were administered by PBMs (as of 2014).[129] However, PBMs have only continued to grow and expand their operations.

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[124] *See Pharmacy Benefit Managers: Practices, Controversies, and What Lies Ahead*, COMMONWEALTH FUND (Mar. 2019), https://www.commonwealthfund.org/sites/default/files/2019-03/Seeley_pharmacy_benefit_managers_ib_v2.pdf; Kathleen Gifford et al., *How State Medicaid Programs are Managing Prescription Drug Costs: Resulting from a State Medicaid Pharmacy Survey for State Fiscal Years 2019 and 2020*, KFF (Apr. 29, 2020), https://www.kff.org/report-section/how-state-medicaid-programs-are-managing-prescription-drug-costs-pharmacy-benefit-administration/.

[125] *Eli Lilly Form 10-K*, SEC at 35, https://www.sec.gov/ix?doc=/Archives/edgar/data/59478/000005947820000057/lly-20191231x10xk.htm.

[126] For example, Eli Lilly boosted its rebate offer to one PBM after it learned of a competitor offering a 54% rebate, 6% annual price protection, and "covering the cost of 'transitioning lives away from Lilly products.'" LLY-SFCOM-UR-00003520, at LLY-SFCOM-UR-00003521; LLY-SFCOM-UR-00003532. *See also* LLY-SFCOM-UR-00002612; LLY-SFCOM-UR-00002644; LLY-SFCOM-UR-00003325.

[127] *Pharmacy Benefit Managers, Early Results on Ventures with Drug Manufacturers*, GAO at 3 (Nov. 1995), https://www.gao.gov/assets/230/221921.pdf.

[128] *Id* at 3.

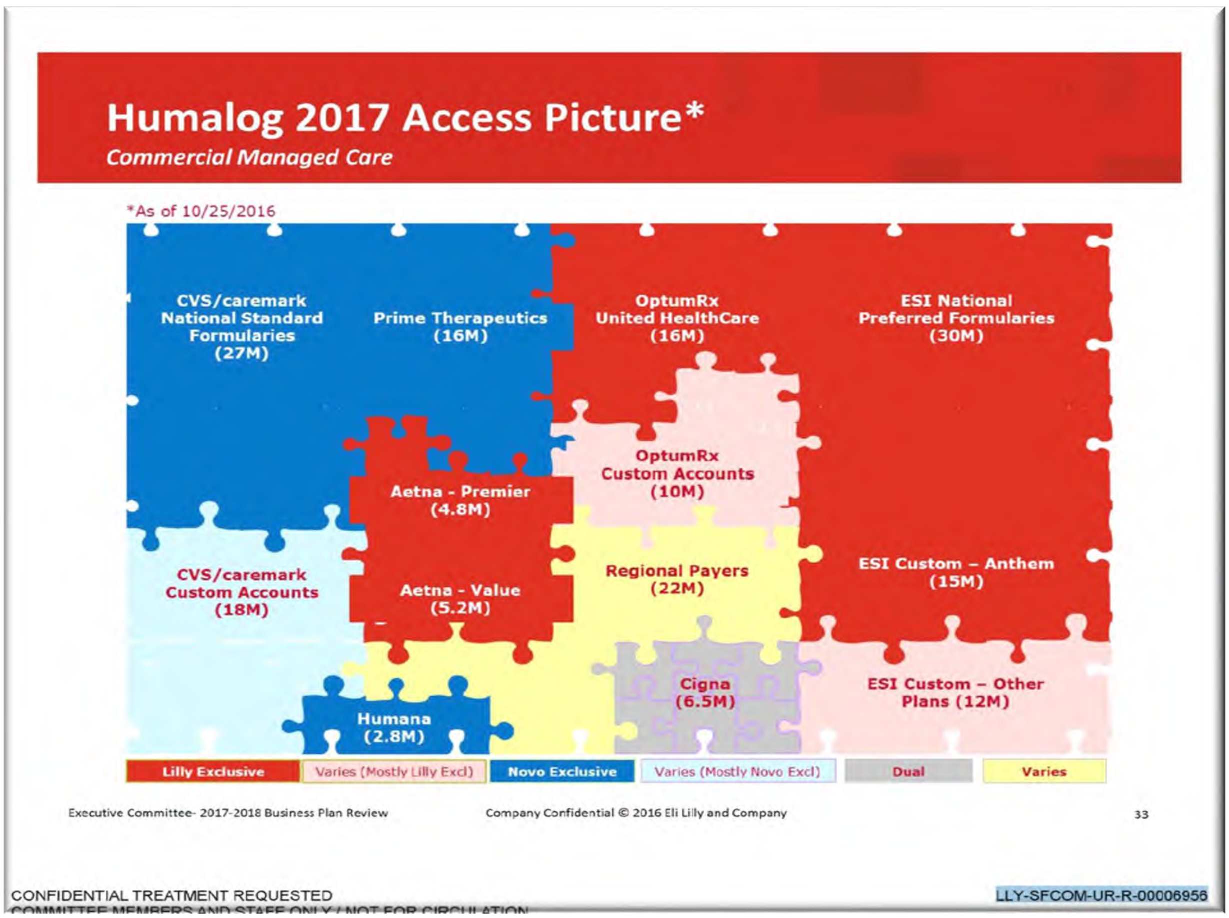
[129] Cole Werble, *Pharmacy Benefit Managers*, HEALTH AFFAIRS (Sept. 14, 2017), https://www.healthaffairs.org/do/10.1377/hpb20171409.000178/full/.

Company	History and Market Position	Proposed Mergers and Partnerships	Total Lives Covered (as of 2019)
CVS Caremark	CVS Health acquires Aetna in November 2018 in a deal worth nearly $70 billion.[130]		105 million.[131]
Express Scripts	In 2018, Cigna acquired Express Scripts in a deal worth approximately $67 billion.[132] In 2012, Express Scripts acquired rival Medco Health Solutions for $29 billion.[133]	In December 2019, Express Scripts announced a partnership with Prime Therapeutics, a PBM collectively owned and operated by 18 Blue Cross Blue Shield health plans, to enhance "pharmacy networks" and "pharmaceutical manufacturer value"—essentially meaning that the PBM will handle negotiations between the health insurer and drug manufacturers.[134]	More than 80 million.[135]
OptumRx	A subsidiary of UnitedHealth Group. In 2015, UnitedHealth Group acquired PBM Catamaran Corp. for		More than 65 million.[137]

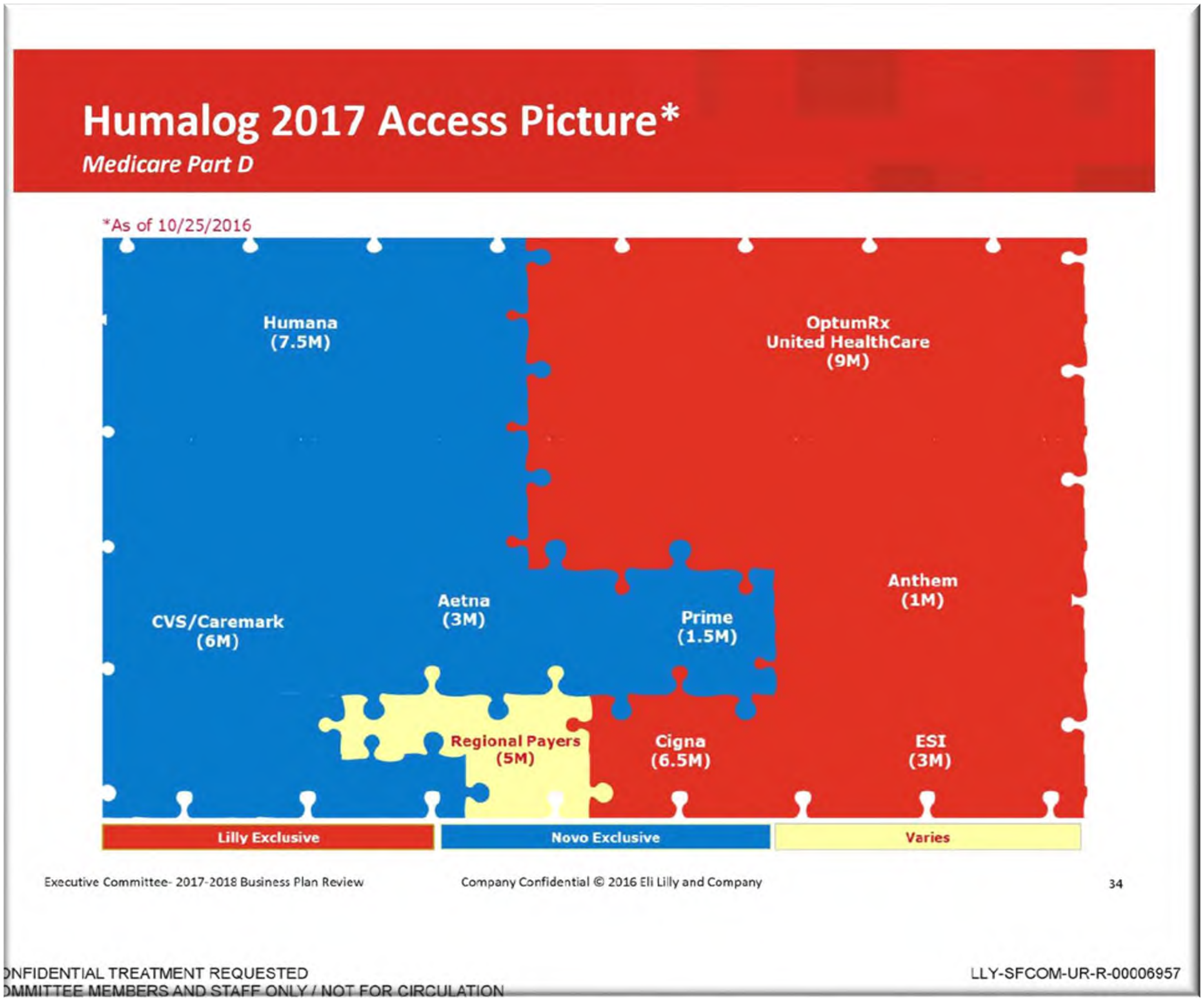
[130] Anna Wilde Mathews and Aisha Al-Muslim, *CVS Completes $70 Billion Acquisition of Aetna*, WALL ST. J. (Nov. 28, 2018), https://www.wsj.com/articles/cvs-completes-70-billion-acquisition-of-aetna-1543423322.
[131] *2019 Annual Report*, CVS HEALTH at 58, https://www.annualreports.com/HostedData/AnnualReports/PDF/NYSE_CVS_2019.pdf.
[132] Press Release, Cigna, Cigna to Acquire Express Scripts for $67 Billion (Mar. 8, 2018), https://www.cigna.com/about-us/newsroom/news-and-views/press-releases/2018/cigna-to-acquire-express-scripts-for-67-billion.
[133] Jaimy Lee, *Express Scripts Buys Medco for $29 Billion*, MODERN HEALTH CARE (Apr. 2, 2012), https://www.modernhealth care.com/article/20120402/NEWS/304029961/express-scripts-buys-medco-for-29-billion.
[134] Press Release, Prime Therapeutics, Express Scripts and Prime Therapeutics Collaborate to Deliver More Affordable Care to More Than 100 Million Americans (Dec. 19, 2019), https://www.primetherapeutics.com/en/news/pressreleases/2019/release-prime-express-scripts-collaboration.html.
[135] Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (Apr. 16, 2019).
[137] *How Did UnitedHealth's OptumRx Revenues Increase in Q3 Despite A Drop in Retail Prescriptions*, FORBES (Nov. 28, 2019), https://www.forbes.com/sites/greatspeculations/2019/11/28/how-did-unitedhealths-optumrx-revenues-increase-in-q3-despite-a-drop-in-retail-prescriptions/?sh=751ad7c42547.

	approximately $13 billion.[136]		

In addition to being the largest PBMs in the country, these companies are also vertically integrated with health insurance companies and operate specialty pharmacies through acquisitions and mergers. For example, OptumRx is a subsidiary of UnitedHealth Group, CVS Caremark is a subsidiary of CVS Health, which acquired the health insurer Aetna in a $69 billion deal in 2018, and Express Scripts merged with health insurer Cigna in 2018.[138] An Eli Lilly presentation prior to the Cigna-Express Scripts and CVS-Aetna mergers suggested that the companies, once combined, would represent 172 million or about 75% of the nearly 228 million people in Part D and commercial markets, alone.[139] Adding the Express Scripts-Prime Therapeutics partnership brings the number to 189.5 million or roughly 83% of those markets.[140] Excerpts from this presentation are shown below.[141]



[136] Anna Wilde Mathews and Joseph Walker, *UnitedHealth to Buy Catamaran for $12.8 Billion in Cash*, WALL ST. J. (Mar. 30, 2015), https://www.wsj.com/articles/unitedhealth-to-buy-catamaran-for-12-8-billion-in-cash-1427709601.
[138] Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (Apr. 16, 2019).
[139] LLY-SFCOM-UR-R-00006924, at LLY-SFCOM-UR-R-00006956-57.
[140] LLY-SFCOM-UR-R-00006924, at LLY-SFCOM-UR-R-00006956-57.
[141] LLY-SFCOM-UR-R-00006924, at LLY-SFCOM-UR-R-00006956-57.



As PBMs have grown, they have faced significant legal scrutiny, including paying millions of dollars in damages, settlements, and fines connected to kickback schemes, fraud allegations, and false claims.[142] Members of Congress and industry groups have expressed

[142] Nate Raymond, *Ohio accuses UnitedHealth's OptumRx of drug overcharges in lawsuit*, REUTERS (Mar. 18, 2019) (emphasizing the significance of current legal scrutiny), https://www.reuters.com/article/us-ohio-drugprices-lawsuit/ohio-accuses-unitedhealths-optumrx-of-drug-overcharges-in-lawsuit-idUSKCN1QZ1UH. *See also 2017 Annual Report*, CVS HEALTH, https://s2.q4cdn.com/447711729/files/doc_financials/annual/annual-report-2017.pdf (last visited Mar. 29, 2019) (noting that CVS reported receiving a civil investigative demand in 2017 from the Attorney General for Washington. The state informed the company that information provided in response to the demand would be shared with California, Florida, Minnesota, New Mexico, and the District of Columbia.); *Express Scripts Form 10-K*, SEC at 32 (Feb. 27, 2018), https://www.sec.gov/Archives/edgar/data/1532063/000153206318000004/esrx-12312017x10k.htm (noting "[Express Scripts] has received inquiries from various state Attorneys General offices in connection with pending investigations into potential unfair and deceptive acts or practices related to the pricing, reimbursement and rebates for insulin and epinephrine products and possible contracts, combinations or conspiracies in restraint of trade in the setting of prices for insulin and epinephrine products" and "[o]n March 29, 2017, the Company received a Civil Investigative Demand from the Office of the Attorney General of Washington related to insulin products."). *Id. See also The State of Competition in the Pharmacy Benefits Manager and Pharmacy Marketplaces, Hearing Before the House Judiciary Comm., Subcomm. on Regulator Reform, Commercial and Antitrust Law*, 114th Cong.

concern that consolidation in the health care sector harms patients and discourages competition. During the Committee's April 9, 2019 hearing titled *Drug Pricing in America: A Prescription for Change, Part III*, Senator Grassley and Senator Wyden questioned CVS Caremark, Express Scripts, and OptumRx executives on anti-competitive behavior and asked that they respond to their concerns that vertical integration may actually harm patients and consumers.[143] In response to Senator Grassley's question, the witnesses pointed to the highly competitive nature of their industry and alluded that vertical integration was required to keep costs low for patients and insurers.[144]

Information collected during this investigation demonstrates that smaller PBMs and rival health insurers with less bargaining power (generally those with fewer patients or "covered lives" served by the company) are offered less generous rebates, discounts, and other fees by drug manufacturers when compared to larger competitors.[145] An example of this dynamic is on display in an internal Sanofi memo regarding its rebate negotiations with a small company, WellDyneRx, LLC, as the company considered offering lower rebates for Lantus and Toujeo, which represented an "opportunity to retain glargine business at WellDyneRx at a lower rebate rate than the national PBM rates."[146] A September 27, 2017 email further elaborated on the company's view:[147]

(2015)(statement of David A. Balto), https://docs.house.gov/meetings/JU/JU05/20151117/104193/HHRG-114-JU05-Wstate-BaltoD-20151117.pdf; Press Release, U.S. Dep't of Justice, Medco to Pay $7.9 Million to Resolve Kickback Allegations, (May 20, 2015), https://www.justice.gov/opa/pr/medco-pay-79-million-resolve-kickback-allegations; Press Release, U.S. Dep't of Justice, U.S. Attorney's Office, Southern District of New York, Manhattan U.S. Attorney Announces $60 Million Civil Fraud Settlement With Accredo Health Group Over Kickback Scheme Involving Prescription Drug (May 1, 2015), https://www.justice.gov/usao-sdny/pr/manhattan-us-attorney-announces-60-million-civil-fraud-settlement-accredo-health-group; Press Release, Attorney General McKenna Announces Caremark To Pay $41 Million To Resolve Multistate Consumer Protection Claims (Feb. 14, 2008), https://www.atg.wa.gov/news/news-releases/attorney-general-mckenna-announces-caremark-pay-41-million-resolve-multistate; Press Release, U.S. Dep't of Justice, Medco to Pay U.S. $155 Million to Settle False Claims Act Cases (Oct. 23, 2006), https://www.justice.gov/archive/opa/pr/2006/October/06_civ_722.html; Press Release, U.S. Dep't of Justice, Justice Department Recovers $1.4 Billion in Fraud & False Claims in Fiscal Year 2005; More Than $15 Billion Since 1986 (Nov. 7, 2005), https://www.justice.gov/archive/opa/pr/2005/November/05_civ_595.html.

[143] *Drug Pricing in America: A Prescription for Change, Part III: Hearing Before S. Comm. on Finance*, 116th Cong. (Apr. 2019) (Question for the record of Sen. Charles E. Grassley, Chairman, S. Comm. Finance).

[144] *Id.*

[145] *See* Press Release, American Medical Association, AMA urges DOJ to challenge CVS-Aetna merger (Aug. 8, 2018), https://www.ama-assn.org/press-center/press-releases/ama-urges-doj-challenge-cvs-aetna-merger.

[146] SANOFI_SFC_00010641.

[147] SANOFI_SFC_00010655.

From: Fondaco, Michael /US
Sent: Wednesday, September 27, 2017 9:32 PM
To: Borys, Margaret /US; Halenar, Lori /US
Subject: RE: Preliminary PRB Agenda 9/28/17

Margaret,

In a nutshell, WellDyneRx is a PBM with ~1M lives. They currently use Gateway as their claims aggregator under ESI. WellDyne believes they can better negotiate rebates on their own instead of getting their rates nipped by both Gateway and ESI. Much more information to be presented tomorrow but the bottom line is the proposed rates are less than the ESI rate so it's a savings to the brand.

Feel free to call me if you have any questions.

Thanks.

Mike

Little more than a month after this email was sent, Sanofi considered offering WellDyneRx rebates between 42% and 50% off WAC for Lantus, and between 40% and 48% off WAC for Toujeo.[148] In comparison, Sanofi prepared a much better offer for CVS's Part D portfolio, which covered 12.8 million lives at the time and was preparing to merge with Aetna, adding another 3.1 million lives. According to internal pricing review board memoranda, on November 30, 2017, Sanofi sought approval to offer rebates up to 72% for Lantus and 67% for Toujeo in addition to administrative fees and deferred payments.[149] A "bid tracker" with rebates Sanofi offered to different payers similarly shows that companies with more "lives" typically received larger discounts than smaller competitors.[150]

What follows is a brief overview of PBM operations based on information collected during the course of the investigation.

i. Formulary Development Process

One of the primary functions that PBMs perform is developing lists of covered drugs for plan sponsors, known as formularies. A formulary is "[a] list of prescription drugs covered by a prescription drug plan or another insurance plan offering prescription drug benefits."[151] Drugs listed on a formulary are typically less expensive for a plan beneficiary to purchase, since they are subject to the plan's drug benefit. In turn, a manufacturer typically provides a rebate to a health plan when a drug is placed on a formulary, saving the plan money on the cost of the medication. A product's formulary placement can also affect a patient's out-of-pocket spending, as demonstrated by an internal Sanofi analysis of Part D formularies operated by CVS Caremark that found co-pays for Lantus could "range . . . from $236 (34% co-ins) to as high as $348 (50% co-ins)" depending on its formulary tier.[152]

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[148] SANOFI_SFC_00010641.
[149] SANOFI_SFC_00009950, at SANOFI_SFC_00009954.
[150] SANOFI_SFC_00010668, at SANOFI_SFC_00010671.
[151] *Formulary*, HEALTHCARE.GOV, https://www.healthcare.gov/glossary/formulary/ (last viewed Dec. 29, 2020).
[152] SANOFI_SFC_00009811, at SANOFI_SFC_00009815.

There are many different types of formularies with different cost-sharing tiers.[153] While each PBM has different names and particular practices for each of its formularies, they all offer their clients a range of options that vary in the amount of restrictions placed on patients (such as step-therapy and prior authorizations), the number of therapies available, and the cost. However, the development of a health plan's formulary is relatively similar across PBMs in that it follows a multi-step process involving several distinct committees within the respective PBMs.

Pharmacy & Therapeutics Committee. The Pharmacy & Therapeutics Committee (P&T Committee) is an independent advisory committee comprised of actively practicing physicians, pharmacists, and other experts who are responsible for evaluating clinical evidence to assess a medication's clinical value.[154] In determining a medication's clinical value, the P&T Committee reviews scientific evidence, medical literature, and standards of practice to assess a medication's safety and efficacy.[155] It then assigns a clinical designation for the drug and makes formulary recommendations for the PBM's "national" formularies (a type of formulary that is designed by the PBM and offered to multiple, sometimes thousands of, plan sponsors) or for an individual client's custom formulary.[156] According to CVS Caremark, Express Scripts, and OptumRx, the P&T Committee neither has access to, nor does it consider, financial factors such

[153] For example, CVS Caremark has several different formularies it offers clients. One such formulary, the "Standard Opt-Out" is the least restrictive, and includes the greatest number of products, with the CVS website noting that it does "not include formulary removals." Troy Brennen, *2018 Formulary Strategy*, CVS CAREMARK (Aug. 1, 2017), https://payorsolutions.cvshealth.com/insights/2018-formulary-strategy. Meanwhile, the "Standard Control" formulary "offers the broadest coverage of generic, brand and specialty medications of [CVS Caremark's] formularies. Updates are made at the beginning of the year with potential quarterly exclusions for hyperinflation and specialty products. It offers savings of 1 to 2 percent on pharmacy spending." *Formulary Management*, CVS CAREMARK, https://payorsolutions.cvshealth.com/programs-and-services/cost-management/formulary-management (last viewed Dec. 29, 2020). The "Value" formulary purports to include only the lowest-cost medications, with CVS Caremark noting it "covers most generics, and select brands, including specialty medications, with tier exceptions or higher copays for non-formulary brands. Drug list and management strategies are updated quarterly. Value Formulary can deliver pharmacy spend savings of up to 8 percent and an increase in generic dispensing of up to 5 percent or more." *Id.* As formularies have become more restrictive, they cost clients less money. CVS Caremark estimated costs for clients with a custom formulary who opted-out of exclusions to be $113.62 per-member per-month (PMPM) whereas the "Value" formulary, which had the highest generic dispensing rate of CVS's various formularies, had the lowest baseline cost at $81.86 per-member-per-month. Jon Roberts, *Trend Drops to the Lowest Level in 4 years, Despite the Headlines, Prescription Spending Growth Slowed for Our Clients*, CVS CAREMARK (Mar. 15, 2017), https://payorsolutions.cvshealth.com/insights/trend-drops-lowest-level-4-years.

[154] *See* Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (Apr.16, 2019); Letter from Michael Bopp, Counsel, Gibson Dunn ,Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (June 21, 2020); Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (Sept. 25, 2019); Letter from Enu Mainigi, Counsel, Williams & Connolly, on Behalf of CVS Health Corp., to Senator Grassley and Senator Wyden (Apr. 26, 2019); Letter from Enu Mainigi, Counsel, Williams & Connolly, on Behalf of CVS Health Corp., to Senator Grassley and Senator Wyden (Aug. 27, 2019); Cigna-SFC-0008830; ORX_Sen_Fin_00001935.

[155] Based on information collected during the Committee's interview with Andy Behm, Vice President of the Office of Clinical Evaluation and Policy, Express Scripts (Nov. 7, 2019). *See also* ORX_Sen_Fin_0005329. (This document, produced by OptumRx, is an example of the type of evidence reviewed by the P&T Committee in making their determination.)

[156] ORX_Sen_Fin_00001935.

as rebates, discounts, or net costs.[157] However, with regard to insulin, the P&T Committee, from a clinical perspective, considers these drugs to be mostly interchangeable.[158]

The P&T Committee also meets annually to review final formulary recommendations.[159] This is often an opportunity to ensure that formularies include products for a wide-range of therapeutic classes and, if necessary, to make final adjustments to plan formularies.[160]

Formulary Development. PBMs also maintain internal committees that determine which therapies are placed on formularies. The development of drug formularies has a major financial impact not only on pharmaceutical companies, but on health insurers and the PBMs. Formulary development committees appear to be at the center of developing these lists. These committees are comprised of company personnel, which may include representatives from formulary management, product management, trade relations, human resources, and clinical account management.[161] PBMs differ in what they call this committee. For example, Express Scripts refers to this committee as the *Value Assessment Committee*, CVS Caremark refers to this Committee as the *Formulary Review Committee*, and OptumRx refers to this committee as the *Formulary Management Committee*.[162] Regardless, their purpose and composition remains similar. What follows is a summary of the operations of OptumRx's Formulary Management Committee (FMC).

OptumRx's FMC meets on a monthly basis and is responsible for reviewing evidence transmitted by the P&T Committee to make formulary placement decisions.[163] The FMC also reviews the "P&T Committee Drug Classification Designations" to make decisions or recommendations about the formulary structure."[164] The P&T Committee can assign one of seven different drug designations, including "essential drug," "essential class," and "optional inclusion" based on clinical evidence.[165] Subject to the clinical designations and recommendations of the P&T Committee, the formulary development committee makes

[157] Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (June 21, 2019); Letter to Senator Grassley and Senator Wyden from Enu Mainigi, Counsel, CVS Caremark (Aug. 27, 2019); ORX_Sen_Fin_00001935, at ORX_Sen_Fin_00001936.
[158] *See* Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (Sept. 25, 2019).
[159] *See* Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (June 21, 2019).
[160] Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (June 21, 2019).
[161] Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (Sept. 25, 2019); Letter from Enu Mainigi, Counsel, Williams & Connolly, on Behalf of CVS Health Corp., to Senator Grassley and Senator Wyden (Apr. 26, 2019); ORX_Sen_Fin_0005387.
[162] Letter from Enu Mainigi, Counsel, Williams & Connolly, on Behalf of CVS Health Corp., to Senator Grassley and Senator Wyden (Apr. 26, 2019); Cigna-SFC-00008830; ORX_Sen_Fin_0005377.
[163] ORX_Sen_Fin_0005377, at ORX_Sen_Fin_0005379.
[164] ORX_Sen_Fin_0005377, at ORX_Sen_Fin_0005378, ORX_Sen_Fin_0005383.
[165] ORX_Sen_Fin_0005377, at ORX_Sen_Fin_0005378, ORX_Sen_Fin_0005383.

formulary recommendations for drugs that are deemed interchangeable[166] by evaluating net cost, rebates, discounts, plan sponsor costs, utilization trends, and business benefit considerations.[167]

Several presentations collected during this investigation demonstrate how the FMC considers the financial impact to OptumRx's business. For example, a FMC presentation dated April 25, 2018, refers to the financial evaluation of different insulin products, such as the net cost and per-member-per-month impact of Humalog;[168] the annual impact on rebates by moving Tresiba to a different formulary tier;[169] the net cost and incremental cost of every insulin product in the long-acting class,[170] and the net WAC of multiple insulin products.[171] This presentation also refers to an FMC vote that was conducted by email,[172] states that "[t]he basal insulin class was evaluated as part of 2019 recontracting (sic) effort to leverage competition and reduce the overall cost of the category,"[173] stresses the need for a "[r]eevaluation of the Humalog brand … to address market dynamics … [and mentions with respect to Humalog that] [a]dditional rebate opportunities [are] available for the various benefit designs."[174]

The materials used for these meetings are provided to, and maintained by, FMC members.[175] The FMC's policies also suggest that the FMC engages in several other types of communications that would have been responsive to the Committee's April 2nd request for information, but that the company failed to produce. For example, OptumRx's FMC policy states:[176]

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166 Some PBMs assign designations to drugs that are clinically similar to other available drug alternatives. For example, Express Scripts' P&T Committee designates insulins as *optional* and forwards this information to the Value Assessment Committee, which evaluates net cost, market share, and drug utilization trends of clinically similar medications. *See* Cigna-SFC-00008330, at Cigna-SFC-00008831. Express Scripts' P&T Committee considers insulins interchangeable. Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (Sept. 25, 2019).

167 *See* Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (June 21, 2020)(stating that Cigna's Value Assessment Committee considers the value of the drug by evaluating net cost, market share, and drug utilization trends of clinically similar medications); Letter from Enu Mainigi, Counsel, Williams & Connolly, on Behalf of CVS Health Corp., to Senator Grassley and Senator Wyden (Apr. 26, 2019)(stating that CVS Caremark's Formulary Review Committee considers net-cost, clinical guidance, marketplace dynamics, and the potential for patient disruption); ORX_Sen_Fin_0005387 (stating that OptumRx's Formulary Management Committee considers net-cost, economic, pharmacoeconomic, and business/benefit considerations as well as factors that are "attractive to current and potential clients, particularly by providing clients with the lowest possible net cost of drugs.")

168 ORX_Sen_Fin_0007468, at ORX_Sen_Fin_0007489.

169 ORX_Sen_Fin_0007468, at ORX_Sen_Fin_0007479.

170 ORX_Sen_Fin_0007468, at ORX_Sen_Fin_0007480

171 ORX_Sen_Fin_0007468, at ORX_Sen_Fin_0007490.

172 ORX_Sen_Fin_0007468, at ORX_Sen_Fin_0007490.

173 ORX_Sen_Fin_0007468, at ORX_Sen_Fin_0007479.

174 ORX_Sen_Fin_0007468, at ORX_Sen_Fin_0007489.

175 ORX_Sen_Fin_0005377, at ORX_Sen_Fin_0005378.

176 ORX_Sen_Fin_0005377, at ORX_Sen_Fin_0005380.

COMMUNICATION
FMC will deliver all approved decisions to SVP of Clinical, and SVP of Industry Relations, for their reference.

FMC will deliver final decisions to the Benefit Implementation Committee ("BIC") for implementation and communication to internal and external stakeholders. Refer to BIC Charter.

PBM clients can also receive documentation concerning formulary recommendations from OptumRx, if their agreement allows for it. (The Finance Committee did not attempt to determine if plans are in fact allowed to review these agreements. However, the Office of Inspector General for the Department of Health and Human Services found that, while some Part D plans have certain contractual rights to audit agreements between their PBMs and manufacturers, they are not always allowed to do so.)[177] The FMC also provides its clients with guidance about how to structure their formularies:[178]

- Clinical Program Strategy: FMC also provides economic guidance into the type of utilization management tools ("UM") for use with particular drugs or a particular Formulary, including, but not limited to, prior authorizations, quantity limits, step therapies, and provider education. FMC makes these decisions by considering clinical, economic and pharmacoeconomic evidence (as available) provided by the P&T Committee, OptumRx staff, and other supporting financial, business and benefit strategy analyses. FMC reviews and considers recommendations and other information, including, but not limited to:

Trade Relations Group. The Trade Relations Group is an internal committee comprised of PBM personnel who are responsible for negotiating or approving rebate agreements with drug manufacturers.[179] PBMs differ in what they call this committee. For example, OptumRx refers to this committee as the Industry Relations Group whereas CVS Caremark and Express Scripts refer to this committee as the Trade Relations Group.[180] For the purposes of this discussion, "Trade Relations Group" will be used. The Trade Relations Group utilizes the PBM's purchasing power and other market forces to negotiate rebates, discounts, and other fees with drug manufacturers.[181] The Trade Relations Group also seeks to obtain the lowest net cost for its clients—regardless of the list price set by manufacturers—and uses certain tactics (e.g., formulary exclusions) to meet its goal.[182]

ii. Rebates, Discounts, and Other Fees

[177] DEP'T HEALTH AND HUMAN SERVS., OFF. OF INSPEC. GEN., CONCERNS WITH REBATES IN THE MEDICARE PART D PROGRAM at 22 (Mar. 11, 2011), https://oig.hhs.gov/oei/reports/oei-02-08-00050.pdf.
[178] ORX_Sen_Fin_0005387.
[179] *See* Letter from Enu Mainigi, Counsel, Williams & Connolly, on Behalf of CVS Health Corp., to Senator Grassley and Senator Wyden (Aug. 27, 2019).
[180] Letter from Enu Mainigi, Counsel, Williams & Connolly, on Behalf of CVS Health Corp., to Senator Grassley and Senator Wyden (Apr. 26, 2019); ORX_Sen_Fin_0004991.
[181] *See* ORX_Sen_Fin_0004991.
[182] ORX_Sen_Fin_0057558.

Rebates are payments made by drug manufacturers to PBMs after the point of sale,[183] and are calculated as a percentage of WAC. Drug manufacturers negotiate rebates with PBMs and health insurers to secure preferred formulary placement for their products.[184] These negotiations can be of such great financial importance to pharmaceutical companies that senior executives up to and including the chief executive officer are often personally involved in the process.[185] Typically, PBMs pass on the majority of these rebates to health insurers,[186] who use rebates to lower premiums, lower cost-sharing, or fund wellness programs for beneficiaries.[187] However, plan sponsors have not always been sufficiently transparent as to how they use rebates, discounts, and other fees they receive from their contracted PBM or from drug manufacturers.[188]

There is limited publicly available information about the contractual arrangements between manufacturers and PBMs. The lack of public understanding stems from the commercial sensitivity of these contracts, and the broad confidentiality clauses that limit their disclosure.[189] The lack of transparency even extends to health plans. While some health plans have certain contractual rights to conduct audits of agreements between their contracted PBM and manufacturers, HHS OIG found that manufacturers can and do refuse such audits.[190]

Moreover, Federal law restricts the dissemination of price and rebate information that companies disclose to the Federal government for Medicaid and Part D plans. Until recently, such information could only be reviewed by the Secretary of the Department of Health and Human Services (HHS), the Comptroller General, Congressional Budget Office, and States (in regards to Medicaid). However, the Consolidated Appropriations Act of 2021 expanded the dissemination of price and rebate information to the Executive Directors of the Medicare Payment Advisory Commission and Medicaid and CHIP Payment and Access Commission—an

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[183] *See* Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (Apr. 16, 2019). CVS Caremark, Express Scripts, and OptumRx all have rebate contracts with the three major insulin manufacturers—Eli Lilly, Novo Nordisk, and Sanofi. Letter Wyden from Michael Bopp, Counsel, Cigna to Senator Grassley and Senator (June 21, 2019); Letter Wyden from Enu Mainigi, Counsel, CVS Caremark to Senator Grassley and Senator (May 24, 2019); ORX_Sen_00001935; ORX_Sen_Fin_0005305.

[184] Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, on Behalf of Sanofi, to Senator Grassley and Senator Wyden (May 24, 2019); ORX_Sen_Fin_0005389. For an example of a rebate agreement, *see* Cigna-SFC-00009847.

[185] e.g., LLY-SFCOM-UR-00005146; LLY-SFCOM-UR-00003868; LLY-SFCOM-UR-00003699; LLY-SFCOM-UR-00003445, LLY-SFCOM-UR-00003449. For example, Eli Lilly's chief executive officer and chief financial officer were personally involved in the approval of multiple rebate offers. At one point, the company's chief financial officer "requested LillyUSA implement a more structured process for executive review of material payer deals (requiring CFO and CEO approval)." *See* LLY-SFCOM-UR-00003445. In another instance, diabetes unit employees were chastised for providing management insufficient time to review rebate deals. *See* LLY-SFCOM-UR-00005146.

[186] In 2019, GAO reported that "PBMs passed nearly all rebates received from manufacturers through to Part D plan sponsors in 2016. Part D plan sponsors reported to CMS that, of the approximately $18 billion in rebates that PBMs negotiated with pharmaceutical manufacturers that year, PBMs retained $74.3 million, or about 0.4%, and passed through the remaining 99.6% to plan sponsors." GOV. ACCT. OFFICE, MEDICARE PART D, USE OF PHARMACY BENEFIT MANAGERS AND EFFORTS TO MANAGE DRUG EXPENDITURES AND UTILIZATION, at 16 (July 2019), https://www.gao.gov/assets/710/700259.pdf .

[187] Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (Apr. 16, 2019); ORX_Sen_Fin_00001935.

[188] *See generally* DEP'T HEALTH AND HUMAN SERVS., OFF. OF INSPEC. GEN., CONCERNS WITH REBATES IN THE MEDICARE PART D PROGRAM (Mar. 11, 2011), https://oig.hhs.gov/oei/reports/oei-02-08-00050.pdf.

[189] SANOFI_SFC_00007985, at SANOFI_SFC_00007994.

[190] DEP'T HEALTH AND HUMAN SERVS., OFF. OF INSPEC. GEN., CONCERNS WITH REBATES IN THE MEDICARE PART D PROGRAM (Mar. 11, 2011), https://oig.hhs.gov/oei/reports/oei-02-08-00050.pdf.

expansion proposed in the Prescription Drug Pricing Reduction Act of 2019 that was introduced by Chairman Grassley and Ranking Member Wyden. And, with regard to public disclosure, the Secretary of HHS is allowed to "disclose (through a website accessible to the public) the weighted average of the most recently reported monthly average manufacturer prices and the average retail survey price determined for each multiple source drug."[191]

The Committee's investigation found that manufacturers negotiate contracts directly with health plans or their PBM representatives. These contracts contain terms for drug-specific rebates, price protection clauses (designed to dissuade manufacturers from implementing large year-over-year WAC increases), and administrative fees charged by PBMs, among other items. The investigation also found that these contracts and subsequent amendments can stretch over hundreds of pages and cover multiple therapies offered by a manufacturer. The base contracts and subsequent amendments are updated frequently—sometimes multiple times a year—often over the course of a decade or more.

Contracts between PBMs and manufacturers provide a menu of options from which their health plans clients can choose certain terms and conditions. Rebates can vary significantly based on utilization and the plan's benefit design. Manufacturers will also typically make multiple rebate offers for each drug, with the size of each offer typically tied to formulary access and competition within a therapeutic class. Often, a higher rebate is offered for preferred formulary placement which may include few, if any, utilization restrictions (i.e., lower cost-sharing for patients or plans agreeing not to implement prior authorization). Manufacturers will also pay higher rebates, and sometimes even an additional rebate, if the health plan agrees to make their drugs the only therapy on a given formulary tier. As this investigation has shown, the size of rebates for the insulin therapeutic class has risen rapidly, with some PBMs securing rebates as high as 70% in recent years. However, it's the PBM or health plan who ultimately decide a drug's formulary placement and the patient's cost-sharing responsibility. (PBMs generate revenue from these negotiations. For example, Cigna retains approximately 5% of these negotiated discounts, since it reported passing on "approximately 95% of rebates, discounts, and price reductions back to our clients.")[192]

In addition to rebates, PBMs negotiate with drug manufacturers for other discounts and fees. One such example is the use of inflationary protection fees (often referred to as price protection). If drug manufacturers raise the WAC beyond a certain agreed upon percentage, price protection is triggered, and manufacturers must pay additional rebates to plan sponsors in addition to rebates and other discounts.[193] As stated previously, plan sponsors use these fees to lower premiums, lower cost-sharing, or fund wellness programs for beneficiaries.[194] (This investigation did not examine the financial relationships between PBMs and plan sponsors.) However, in 2011, HHS OIG raised concerns that Part D sponsors "commonly had complex

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[191] *See* 42 U.S.C. 1396r-8(b)(3)(D)(cross-referenced at 42 U.S.C. 1395w-102(d)(2) and 42 U.S.C. 1396r-8(b)(3)(D)).
[192] Letter from Kristin Julason Damato, Vice President, Global Public Policy & Government Affairs, Cigna Corporation, to Senator Grassley and Senator Wyden (Dec. 7, 2020).
[193] Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (Apr. 20, 2019); Letter from Enu Mainigi, Counsel, Williams & Connolly, on Behalf of CVS Health Corp., to Senator Grassley and Senator Wyden (May 24, 2019); ORX_Sen_Fin_00001935; ORX_Sen_Fin_0005389.
[194] Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (Apr. 16, 2019); ORX_Sen_Fin_00001935.

relationships with their PBMs, and in some cases, these relationships lacked transparency," which "raises concerns that sponsors may not always have enough information to oversee the services and information provided by PBMs."[195] HHS OIG added:

> Five sponsors had limited information about the rebate contracts and the rebate amounts negotiated by their PBMs. One PBM reported that it does not share the manufacturer rebate contracts with its sponsors because they contain confidential information and there is a chance that the sponsor may one day become a PBM itself. Another PBM specifically stated that the sponsor would 'not be permitted to copy or retain' any portion of the contract. As a result of these practices, most of the selected sponsors were unaware of all of the contract terms that determine the rebates they receive from drug manufacturers.[196]

The following information details the Committee's findings based on internal documents and memoranda collected from manufacturers (Sanofi, Novo Nordisk, and Eli Lilly) and PBMs (CVS Caremark, Express Scripts, and OptumRx), and seeks to shed further light on these contractual relationships, the negotiations that take place between these two groups, and how rebates, discounts, and fees contribute to insulin's rising list price.

III. The Cost of Insulin to Patients, Medicare, and Private Payers

Increases in insulin's list price have dramatically exceeded rates of inflation and health care inflation,[197] leading to concerns about affordability and access for patients. Indeed, during the Committee's hearing titled: *Drug Pricing in America: A Prescription for Change Part I*, the Committee heard from Kathy Sego, a resident of Indiana and a mother whose son has Type 1 diabetes.[198] Ms. Sego told the Committee how, unbeknownst to her, her son rationed his insulin so that their family could afford the $1,700 price tag of his monthly insulin medication. It wasn't until he stopped eating, lost 20 pounds, and seemed depressed that she realized that something was wrong. Unfortunately, Ms. Sego's family is not alone in this struggle. Therefore, as Congress considers common sense policy solutions to address this growing crisis, it is critically important to understand how insulin's list price has evolved over time, and the various factors and players that have caused it to increase exponentially in the past decade.[199]

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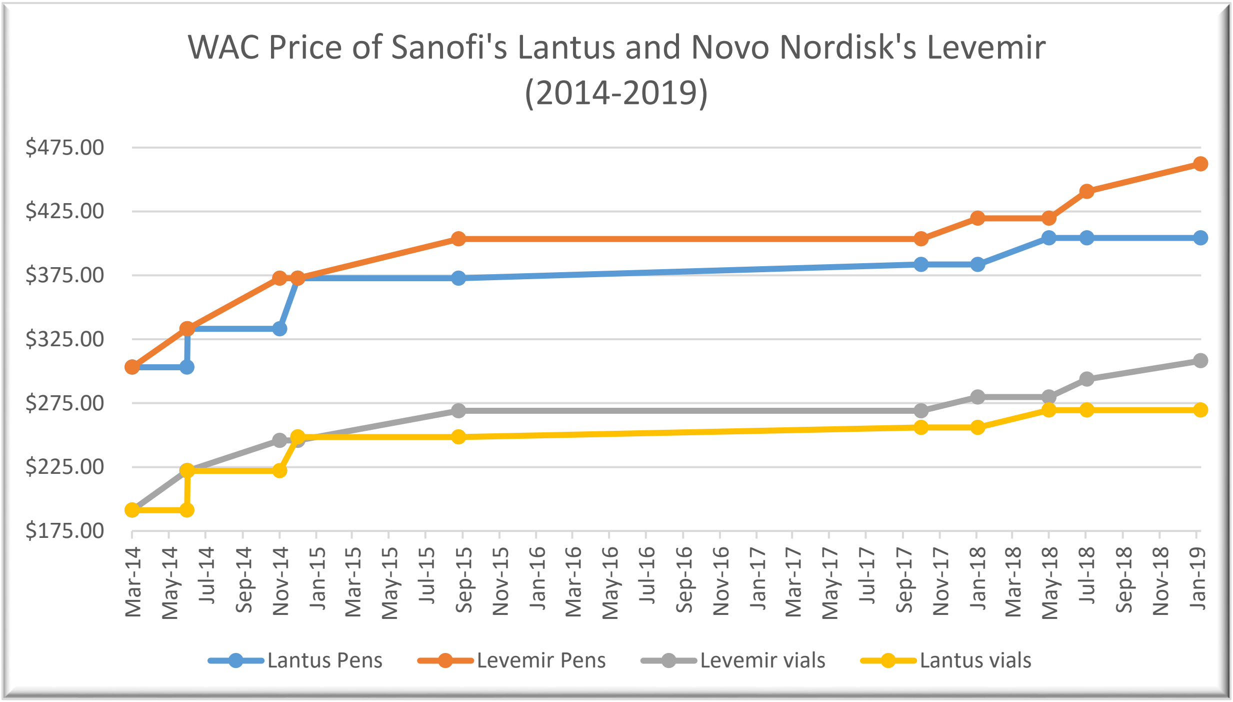
[195] DEP'T HEALTH AND HUMAN SERVS., OFF. OF INSPEC. GEN., CONCERNS WITH REBATES IN THE MEDICARE PART D PROGRAM, at 17 (Mar. 11, 2011), https://oig.hhs.gov/oei/reports/oei-02-08-00050.pdf.
[196] Id. AT 17-18.
[197] *National Health Expenditure Projections, 2019-2028*, CTRS. MEDICARE AND MEDICAID SERVS., https://www.cms.gov/files/document/nhe-projections-2019-2028-forecast-summary.pdf (last viewed Dec. 28, 2020) (The rate of personal health care inflation is projected to grow 1.9% in 2020 up from 1.5% in 2019). According to the Keiser Family Foundation: "Among the 22 insulin therapies that have been on the market since 2013, 16 products had average annual increases of more than 10% between 2014 and 2018 . . . which far exceeded the 1.5% rate of inflation over the same time period." *Insulin Costs and Coverage in Medicare Part D*, KFF (June 2020), https://www.kff.org/report-section/insulin-costs-and-coverage-in-medicare-part-d-issue-brief/.
[198] *Drug Pricing in America: A Prescription For Change Part I, Hearing Before the S. Fin. Comm*., 116th Cong. (2019) (statement of Kathy Sego), https://www.finance.senate.gov/imo/media/doc/29JAN2019SEGOSTMNT.pdf.
[199] The *Prescription Drug Price Reduction Act of 2020* (co-authored by Senator Grassley and Senator Wyden) is one such piece of legislation that would reduce prescription drug costs for Americans. *See* Press Release, Grassley, Colleagues Introduce Updated Bipartisan Prescription Drug Pricing Bill (July 2, 2020), https://www.grassley.senate.gov/news/news-releases/grassley-colleagues-introduce-updated-bipartisan-prescription-drug-pricing-bill.

a. Insulin List and Net Price Trends: 2013 to 2019

Drug manufacturers independently set the price for their medications—referred to as wholesale acquisition cost, WAC, or list price—based on a number of factors.[200] Documents reviewed during this investigation show that the primary factors considered by companies were the competitive environment, the need to provide rebates, discounts, and other fees to health insurers and their PBMs, and the importance of maintaining market access to preserve sales volume and revenue. When manufacturers set the WAC price for a given product, it is applicable to all payer contracts in its book of business. However, the WAC price is not the amount the manufacturer receives, nor is it the amount paid by the Federal government, health insurers, or employers. The WAC price is the starting point that manufacturers use to negotiate with wholesale distributers, who resell the medication to pharmacies.[201] Instead, manufacturers receive what is known as "net price," which is the amount of money remaining after the manufacturer pays for rebates, discounts, and other fees to health insurers or PBMs, Federal and state health care programs, employers, and other entities.[202]

The following tables refects the WAC price of Sanofi's Lantus and Novo Nordisk's Levemir between 2014 and 2019.[203]

[200] Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, on Behalf of Sanofi, to Senator Grassley and Senator Wyden (Mar. 8, 2019); Letter from Raphael Prober, Counsel, Akin Gump, on Behalf of Novo Nordisk, to Senator Grassley and Senator Wyden (Mar. 8, 2019); Letter from Joseph B. Kelley, Vice President, Global Government Affairs, Eli Lilly, to Senator Grassley and Senator Wyden (Mar. 8, 2019).
[201] Letter from Joseph B. Kelley, Vice President, Global Government Affairs, Eli Lilly, to Senator Grassley and Senator Wyden (Mar. 8, 2019).
[202] *Id.* The practical effect of rebates is substantial. For example, Novo Nordisk reported net sales of DKK 122 billion (Danish krone) in 2019, noting in its annual report, "the provision for sales rebates and discounts amounted to DKK 30,878 million as of December 31, 2019, *of which a significant portion relates to the US business*." *2019 Annual Report*, NOVO NORDISK, https://www.novonordisk.com/content/dam/nncorp/global/en/annual-report/pdfs/2019/Novo-Nordisk-Form-20-f-2019.pdf (last viewed Dec. 29, 2020).
[203] Calculated using WAC data produced by Sanofi and Novo Nordisk. Sanofi produced WAC data for insulin products per milliliter. In order to calculate the WAC total, Committee staff multiplied price per milliliter by the amount of mL in the vial or in the box. *See* Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, on Behalf of Sanofi, to Senator Grassley and Senator Wyden (Mar. 8, 2019) (attachment 1(a) and (b)). NNI-FINANCE-0002-03.



This investigation primarily focused on the change in WAC price between three long-acting insulins[204]—Lantus, Levemir, and Basaglar—that are in direct competition with each other. Sanofi and Novo Nordisk have steadily increased Lantus' and Levemir's WAC since 2005.[205] Based on WAC data tracked in internal documents, between 2013 and 2019, Lantus' and Levemir's WAC prices increased rapidly.[206] For example:

- Sanofi's Lantus SoloStar (pens) increased from a WAC of $303 in January 2014 to approximately $404 in January 2019—an increase of over 33% in 5 years.[207]

- Novo Nordisk's Levemir Flextouch (pens) increased from a WAC of $303 in May 2014 to approximately $462 in January 2019—an increase of over 52% in 5 years.[208]

[204] According to the ADA, "long-acting insulin reaches the blood stream several hours after injection" and keeps glucose levels stable in the body for up to 24 hours. *See Insulin Basics*, ADA, https://www.diabetes.org/diabetes/medication-management/insulin-other-injectables/insulin-basics (last visited Dec. 29, 2020).
[205] E.g., Sanofi increased Lantus's WAC by almost 250% from 2005 to 2015, while retaining higher average net prices. *See* SANOFI_SFC_00009556. (On file with Committee). *See also* SANOFI_SFC_00009527.
[206] *See* Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, on Behalf of Sanofi, to Senator Grassley and Senator Wyden (Mar. 8, 2019) (attachment 1(a) and (b)). NNI-FINANCE-0002-03.
[207] Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, on Behalf of Sanofi, to Senator Grassley and Senator Wyden (Mar. 8, 2019) (attachment 1(a) and (b)).
[208] NNI-FINANCE-0002-03.

- Eli Lilly's Basaglar launched in November 2016 with a WAC price 23% lower than Lantus at $316.85.[209] However, Basaglar's WAC price increased to $326.36 the following year.[210]

List prices for short-acting and rapid-acting insulins have also risen dramatically during this time period.[211] For example, in 2017, Eli Lilly's Humalog 50-50 Kwikpen[212] had a WAC of $530.40 compared to $323.95 in 2013—representing an increase of approximately 64% in 4 years.[213] Sanofi's rapid-acting insulin, Apidra, increased from $302 in 2014 to $521 in 2019, and Novo Nordisk's rapid acting insulin, Novolog Mix 70/30 FlexPen, increased from $324 in 2013 to $558 in 2018, over a 70% WAC increase for both companies during this time.[214]

While insulin manufacturers set a single WAC price for each product across their entire book of business, it is important to note that there is no "single" net price for insulin.[215] As discussed above, manufacturers negotiate contracts with PBMs that provide participating health plans with a range of rebates and other discounts based on, and subtracted from, the product's WAC price. The contracts stipulate terms the plans must follow regarding factors such as formulary placement and competition from other drugs in the therapeutic class. As such, a manufacturer can actually receive multiple net prices from a single payer if the payer operates multiple plans that, in turn, place the product in different formulary positions.[216]

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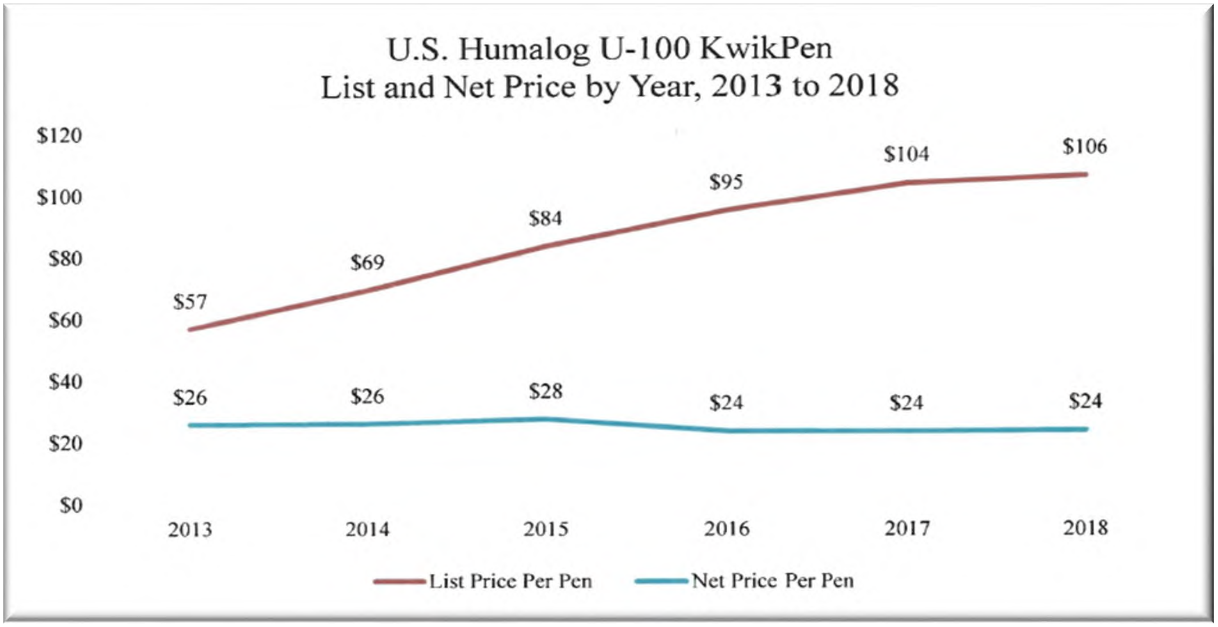
[209] LLY-SFCCOM-00000001. *See also* Letter from Joseph B. Kelley, Vice President, Global Government Affairs, Eli Lilly, to Senator Grassley and Senator Wyden (Mar. 8, 2019).
[210] LLY-SFCCOM-00000001.
[211] As discussed above, there are several different kinds of insulin products. According to the ADA, rapid-acting insulins begin to work about 15 minutes after injection (e.g., Fiasp, NovoLog, Apidra, Admelog, and Humalog). Short-acting insulins on the other hand reach the bloodstream within 30 minutes after injection (e.g., Humulin R, Novolin R). *See Insulin Basics*, ADA, https://www.diabetes.org/diabetes/medication-management/insulin-other-injectables/insulin-basics (last viewed Dec. 29, 2020).
[212] Specifically, Humalog Kwikipen U-100.
[213] LLY-SFCCOM-00000001.
[214] *See* Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, on Behalf of Sanofi, to Senator Grassley and Senator Wyden (Mar. 8, 2019) (attachment 1(a) and (b)). NNI-FINANCE-0002-03.
[215] *See* Letter from Reginald Brown, Counsel, WilmerHale, on Behalf of Eli Lilly, to Senator Grassley and Senator Wyden (Mar. 8, 2019).
[216] Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, on Behalf of Sanofi, to Senator Grassley and Senator Wyden (Mar. 8, 2019); Letter from Raphael Prober, Counsel, Akin Gump, on Behalf of Novo Nordisk, to Senator Grassley and Senator Wyden (Mar. 8, 2019); Letter from Joseph B. Kelly, Vice President, Global Government Affairs, Eli Lilly, to Senator Grassley and Senator Wyden (Mar. 8, 2019).



Data and documents produced to the Committee suggest that the net prices of insulin manufacturers' products has declined in recent years, but remained significantly higher than they were in the first decade of the 21st Century. For example, in a letter to the Committee, Eli Lilly provided data showing that its average net price for Humalog KwikPen had declined slightly from $28 per pen in 2015 to $24 per pen in 2018, despite the WAC price nearly doubling during that same period (see figure above).[217] On the other hand, an internal Sanofi presentation shows that while the average Lantus net price of $87.48 in 2016 was $32 lower than the drug's net price in 2014, it was roughly double the drug's net price of $46.92 in 2005.[218] Net price growth was also significantly greater than the Consumer Price Index growth the company tracked.[219] An excerpt of Sanofi's internal presentation is shown below.[220]

[217] Letter from Joseph B. Kelly, Vice President, Global Government Affairs, Eli Lilly, to Senator Grassley and Senator Wyden (Mar. 8, 2019).
[218] SANOFI_SFC_00011407, at SANOFI_SFC_00011416.
[219] SANOFI_SFC_00011407, at SANOFI_SFC_00011416.
[220] SANOFI_SFC_00011407, at SANOFI_SFC_00011416.

Lantus Price Evolution

	NS	VOL	Price	WAC	GTN	CPI	CPI Growth	Act Growth	Δ	WAC	Net	Growth vs 2007	
2005						3%				57.35	46.92		
2006	40%	19%	20%	15%	5%	3%	29	184	155	64.67	54.97		
2007	30%	17%	13%	13%	0%	3%	35	167	132	71.96	61.22	WAC	NET
2008	31%	16%	14%	18%	-3%	4%	62	236	174	83.04	68.81	15.4%	12.4%
2009	24%	14%	10%	12%	-3%	0%	(9)	207	215	91.95	74.66	27.8%	22.0%
2010	7%	4%	3%	10%	-7%	2%	42	76	34	100.64	76.72	39.9%	25.3%
2011	15%	11%	4%	10%	-6%	3%	91	109	18	109.98	79.37	52.8%	29.7%
2012	22%	6%	16%	19%	-4%	2%	68	508	439	130.05	91.03	80.7%	48.7%
2013	26%	7%	19%	25%	-6%	2%	59	754	694	160.16	107.27	122.6%	75.2%
2014	12%	1%	11%	35%	-24%	2%	80	563	484	215.74	119.28	199.8%	94.8%
2015	-20%	1%	-21%	15%	-37%	0%	6	(1,202)	(1,208)	248.41	93.97	245.2%	53.5%
2016	-13%	-6%	-6%	0%	-7%	1%	45	(290)	(334)	248.45	87.48	245.2%	42.9%
							$ 304	$ 731	$ 428				

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It is clear that WAC prices have not kept up with the growing size of rebates, discounts, and other fees, putting pressure on pharmaceutical manufacturers' margins. The Committee found examples of manufacturers recognizing this market dynamic and seeking to make up for lost revenue elsewhere. For example, in 2014, senior officials in Eli Lilly's diabetes business unit were preparing to warn company executives "that the ability to pull the US price lever for Humalog to cover a gap in the overall corporate plan does not exist."[221] Another employee in the exchange observed, "[t]his is an interesting picture –list prices going way up and so are rebates– after these major changes … our net prices are flat."[222] His colleague responded, "Exactly. And to expect it to grow again in a meaningful way would be a huge planning risk."[223]

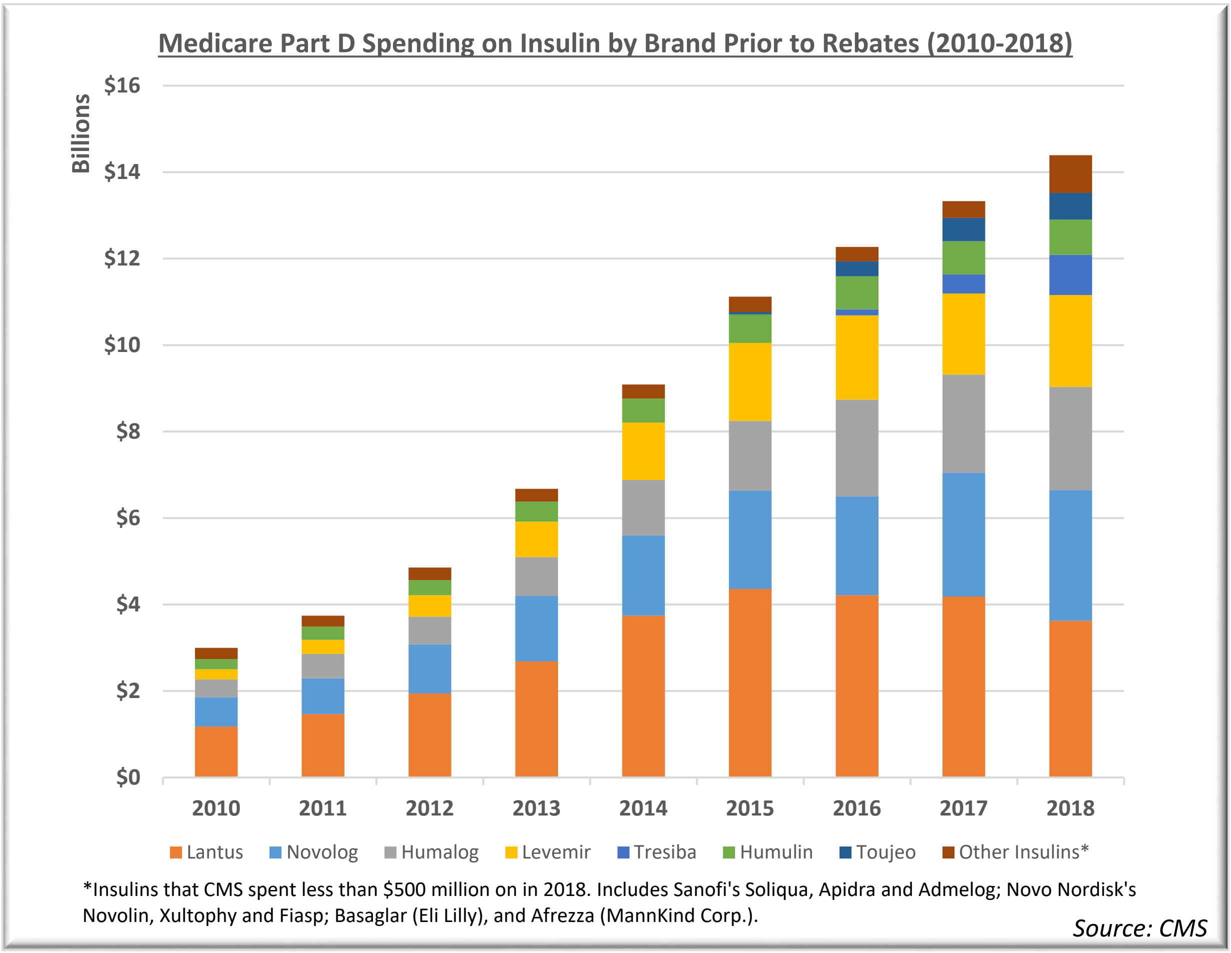
b. Medicare Part D's Pre-Rebate Spending on Insulin has Risen Steadily Since 2010

CMS provided the Finance Committee with data that show the growing amount of money that Medicare Part D plans have paid for insulin, prior to rebates and other discounts, since 2010. Rebates negotiated by Part D plans are treated as confidential information by Federal law,

[221] LLY-SFCOM-UR-00003170.
[222] LLY-SFCOM-UR-00003170.
[223] LLY-SFCOM-UR-00003170.

therefore, this analysis examines spending before rebates.[224] Spending before rebates is an important data point to consider, as patients' out-of-pocket costs are affected in part by a drug's WAC price before rebates, discounts, and other fees are included.

Based on data provided by CMS, annual spending on insulin has increased by billions of dollars over the last decade. Between 2010 and 2018, Medicare Part D spent $78.4 billion on insulin prior to rebates, the majority of which was spent on Lantus ($27.4 billion), Novolog ($16.5 billion), Humalog ($12.3 billion), and Levemir ($11 billion).[225]



The growth of CMS's pre-rebate spending on insulin also significantly outstripped the growth rate of beneficiaries utilizing insulin from 2010 to 2018. For instance, the number of Part

[224] According to Medicare actuaries, the average rebate negotiated by Medicare Part D plan sponsors for all drugs has increased substantially in recent years. 2020 ANNUAL REPORT OF THE BOARDS OF TRUSTEES OF THE FEDERAL HOSPITAL INSURANCE AND FEDERAL SUPPLEMENTARY MEDICAL INSURANCE TRUST FUNDS (2020), https://www.cms.gov/files/document/2020-medicare-trustees-report.pdf.

[225] During this investigation, the Committee received data from CMS on insulin spending on Medicare Part B and D. Spending for Medicare Part B drugs also increased between 2010 and 2018. For example, in 2010, the Federal government spent $14 million prior to rebates on insulin drugs administered by a physician and covered by Medicare Part B. By 2018, the Federal government reported spending over $96 million prior to rebates on Medicare Part B insulin payments—representing an increase of approximately 585% in less than 8 years.

D beneficiaries using insulin increased 51%, from over 2.1 million in 2010 to approximately 3.2 million in 2017, whereas spending on insulin prior to rebates increased more than 470%, from over $3 billion in 2010 to roughly $14.3 billion in 2018. To put this into perspective, the $11 billion increase in pre-rebate annual spending on insulin over those eight years is roughly equal to the total proposed budget of the Federal Transit Administration for Fiscal Year 2021.[226]

c. Patient Out-of-Pocket Spending in Medicare Part D

As noted above, rising WAC prices can increase a patient's out-of-pocket costs. However, out-of-pocket costs vary widely due to multiple factors, including WAC price, dosage quantity, days' supply, formulary and utilization management decisions made by the health plan, and the relevant coverage phase of the Part D benefit.[227] A recent study published in *The New England Journal of Medicine* breaks down the considerable costs faced by Part D beneficiaries using insulin:

> When examining strategies for making insulin more affordable for older adults, it is important to consider how Part D plans currently cover insulin. Of the 3649 outpatient prescription-drug plans that were available to Medicare beneficiaries (Part D plans) in 2019, we found that nearly 90% offered long-acting insulin products (the most commonly used insulin in Part D) with copayments ranging from $45 to $47 per fill in the initial coverage phase (up to $4,020 in total drug spending in 2020) of the Part D benefit. We expect benefit designs to be similar for 2020 plans. Thus, for beneficiaries with less than $4,020 in total drug spending in 2020, copayments would be used for every insulin fill. For beneficiaries with more than $4,020 in total drug spending (average monthly drug costs of more than $335), nearly all plans required 25% coinsurance in the Part D coverage gap, with median out-of-pocket costs ranging from $72 to $236 per fill in this benefit phase. Considering average list prices, patients with typical Part D plans who use long-acting insulin and have no other drug expenditures would spend $1,140.68 out of pocket on 12 fills of insulin ($46.00 per fill for about 6.5 fills in the initial coverage phase and $153.75 per fill for the remaining fills in the coverage gap).[228]

However, a patient's out-of-pocket costs are likely higher, as a majority of diabetics also utilize short-acting, rapid-acting, and/or intermediate-acting insulins, buy test-strips and other medical devices, and take medications for other comorbidities (e.g., hypertension or renal disease).[229] Indeed, based on Part D gross drug cost data collected from CMS, in 2018, more than a quarter of patients enrolled in Medicare Part D spent upwards of $5,000 a year on their

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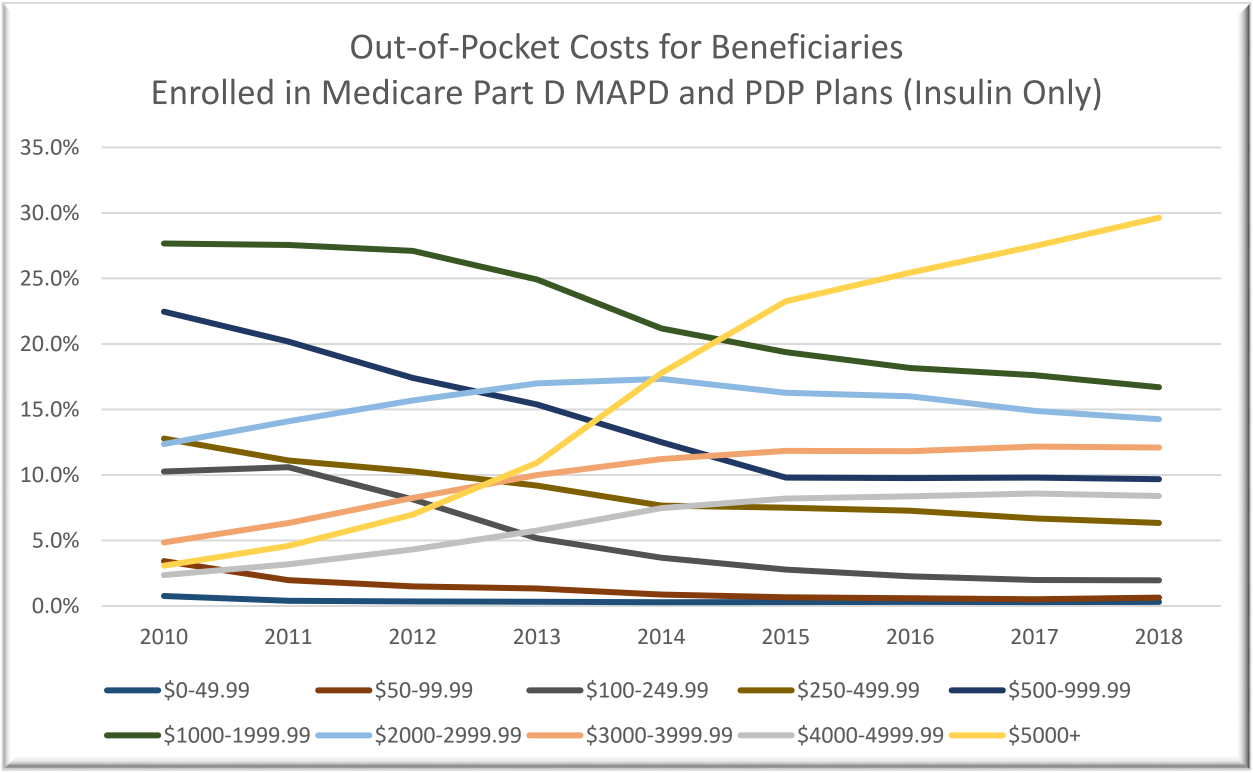
[226] *See* PRESIDENT DONALD J. TRUMP'S FY 2021 BUDGET TITLED: A BUDGET FOR AMERICA'S FUTURE, https://www.whitehouse.gov/wp-content/uploads/2020/02/budget_fy21.pdf.
[227] Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (Apr. 20, 2019).
[228] Stacie B. Dusetzina et al., *Medicare Part D and Insulin Affordability—The Devil is in the Details*, N. ENG. J. MED. 1878, 1878 (Apr. 1, 2020).
[229] *Type 1 diabetes*, MAYO CLINIC, https://www.mayoclinic.org/diseases-conditions/type-1-diabetes/diagnosis-treatment/drc-20353017(last viewed Jan. 4, 2021); *Type 2 diabetes*, MAYO CLINIC, https://www.mayoclinic.org/diseases-conditions/type-2-diabetes/diagnosis-treatment/drc-20351199 (last viewed Jan. 1, 2021).

insulin medications.[230] This represents a dramatic increase in out-of-pocket spending compared to 2010 where a majority of Medicare Part D patients spent $2,000 or less.



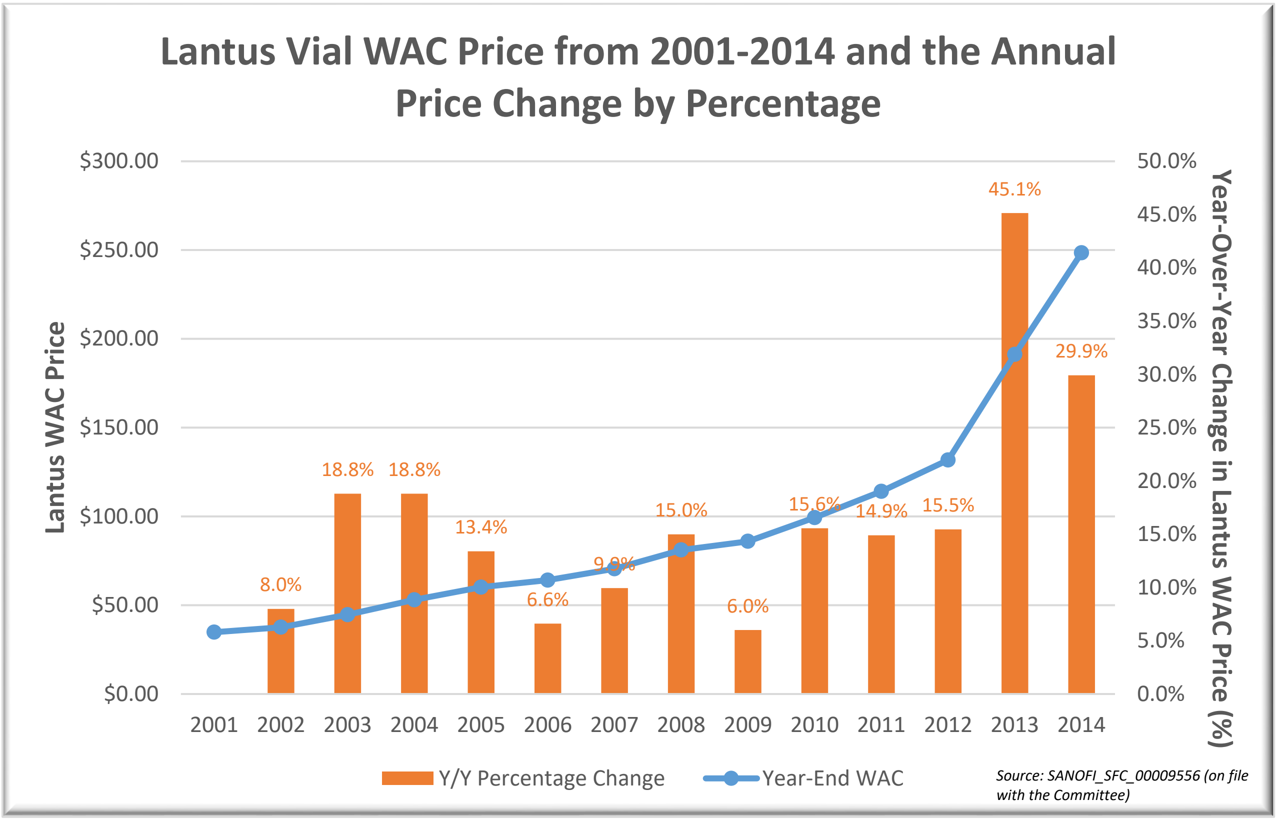
Documents produced to the Committee show that rebates, administrative fees and other price concessions are significant factors affecting how manufacturers determine WAC prices. In the insulin therapeutic class, PBMs consider insulins to be interchangeable in their safety, efficacy, and kinetics.[231] It has also become increasingly common for PBMs and health insurers to offer only one line of insulin products on their formularies while excluding the rest.[232]

d. A Case Study: Examining Sanofi and Novo Nordisk's Decision to Implement Aggressive List Price Increases and the Impact on the Long-acting Insulin Market

Sanofi's decision to significantly increase Lantus's list price between 2001 and 2014 contributed to the dramatically increasing cost of long-acting insulins over the past decade. Sanofi manufactures two long-acting insulins under the trade names Lantus and Toujeo,[233] in

[230] During this investigation, we collected data from CMS on insulin spending on Medicare Part C and D gross drug costs by coverage type. Medicare Part D prescription drug events contain prescription drug costs and payment data that enable CMS to make payments to plans. Using this data, CMS was able to calculate gross drug costs for insulin drugs from 2012 through 2018.
[231] *See* Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (Apr. 16, 2019).
[232] Letter from Joseph B. Kelly, Vice President, Global Government Affairs, Eli Lilly, to Senator Grassley and Senator Wyden (Mar. 8, 2019).
[233] Sanofi manufactures insulin glargine, a type of long-acting insulin that mimics the flat profile of insulin released from a healthy pancreas. *See* Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, to Senator Grassley and Senator Wyden (Mar. 8, 2019).

addition to rapid-acting insulins Apidra and Admelog (a biosimilar of the mealtime insulin Humalog).[234] According to internal documents and correspondence acquired by the Committee, Sanofi's intent behind Lantus's price increase centered on its objective to maximize profits, ensure the overall long-term success of its diabetes franchise, and respond to aggressive rebate and discount activity from Novo Nordisk and PBMs.[235]



According to internal data, Lantus's WAC price was $34.81 in 2001.[236] See graph above. From 2005 to 2011, internal memoranda show Sanofi increased Lantus's list price as much as 18% annually.[237] However, between 2012 and 2014, Sanofi increased Lantus's list price at a rate significantly higher than it had done previously. For example, Sanofi increased Lantus's list price three times in 2013 alone—on April 26, 2013, August 2, 2013, and December 13, 2013—resulting in a total increase of approximately 39.7% for Lantus vials and 29.7% for Lantus pens.[238] Data provided to the Committee by Sanofi show the company increased Lantus's price two more times in 2014 and, by December 1, 2014, Lantus cost $248.51 per vial, and Lantus pens cost $372.76 per package.[239] However, Sanofi's decision to increase Lantus's list price was

[234] *See* Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, to Senator Grassley and Senator Wyden (Mar. 8, 2019).
[235] SANOFI_SFC_00009132, at SANOFI_SFC_00009135.
[236] SANOFI_SFC_00009556.
[237] This figure represents Lantus's average WAC increase between 2005 and 2011 on a percentage basis. *See* SANOFI_SFC_0011407, at SANOFI_SFC_00011416.
[238] SANOFI_SFC_00014580, at SANOFI_SFC_00014582; NNI-FINANCE-001699, at NNI-FINANCE-001701.
[239] *See* Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, to Senator Grassley and Senator Wyden (Mar. 8, 2019) (attachment 1(a) and (b)).

not without consequences. In the run-up to rebate negotiations with Express Scripts in 2015, Sanofi noted that "Lantus price increases over the past two years have positioned Sanofi as a cost driver that has triggered significant attention from [Express Scripts]."[240]

According to an internal memo created by Sanofi in 2013/2014, the company took aggressive pricing actions for several reasons. First, Sanofi sought to retain as many diabetes patients as possible in advance of future pipeline expansion and product competition and, in 2013, decided to close the price differential between Lantus vials and Lantus pens on a per unit basis.[241] By setting a single price point for Lantus, and by launching Toujeo—its next-generation concentration of insulin glargine—at WAC parity to Lantus, Sanofi believed that it would remove cost as a barrier for switching patients to Toujeo to become the preferred basal insulin.[242] The diabetes franchise was—and remains—extremely important to the company, with Sanofi describing Lantus as a "flagship product" of its diabetes division, accounting for revenue of €4.9 billion in 2013, equal to 14.2% of the company's revenue that year.[243] According to Sanofi, if Lantus were to encounter product challenges, such as pressure from existing competitive products or a reduction in sales, the adverse impact to Sanofi's business "could be significant."[244]

Second, Sanofi raised Lantus's list price to respond to rebate and discount competition from Novo Nordisk. Novo Nordisk manufactures two long-acting insulins under the trade names Levemir and Tresiba as well as two rapid-acting insulins NovoLog and Fiasp.[245] In the long-acting insulin category, Lantus and Levemir often compete to win the same accounts. According to internal memoranda, in 2013, Sanofi believed that Novo Nordisk was attempting to minimize the clinical difference between Lantus and Levemir and was offering "increased rebates and/or portfolio offers for the sole purpose of removing Lantus from favorable formulary access."[246] According to an internal Sanofi memo, "the strategy to close the price differential between the Lantus vial and pen before the LOE [loss of exclusivity] period was believed to be critical to the overall long-term success of the franchise."[247]

Third, Sanofi also faced increased pressure from its payer and PBM clients to offer more generous rebates and price protection terms or face exclusion from formularies, developments that were described as "high risk for our business" that had "quickly become a reality."[248] These insurance market changes were partly driven by the implementation of the ACA, which put pressure on plan margins, and a willingness by plans to exclude drugs from their formularies as a negotiating tool.[249] This market environment created an enormous challenge for Lantus and, in order to protect its flagship diabetes franchise, Sanofi appears to have increased Lantus's list

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[240] SANOFI_SFC_00014648, at SANOFI_SFC_00014653.
[241] SANOFI_SFC_00009132, at SANOFI_SFC_00009135.
[242] SANOFI_SFC_00009377, at SANOFI_SFC_00009378, SANOFI_SFC_00009388-89.
[243] Sanofi 20-F, page 8 (2013). Sanofi reported revenue to the Securities and Exchange Commission in Euros. €4.9 billion is approximately $5.96 billion in today's dollars.
[244] Sanofi 20-F, page 8 (2019); Sanofi 20-F, page 8 (2013).
[245] *See* Letter from Raphael Prober, Counsel, Akin Gump, on Behalf of Novo Nordisk, to Senator Grassley and Senator Wyden (June 28, 2019).
[246] *See* SANOFI_SFC_00009211, at SANOFI_SFC_00009217. Sanofi believed that Novo Nordisk was offering rebates as high as 53% on Levemir during this time. SANOFI_SFC_00009132, at SANOFI_SFC_00009140.
[247] SANOFI_SFC_00009132, at SANOFI_SFC_00009135.
[248] SANOFI_SFC_00009132, at SANOFI_SFC_00009135.
[249] SANOFI_SFC_00009132, at SANOFI_SFC_00009132-33.

price so that it could improve its rebate and discount offering to payers while maintaining net sales.

Sanofi understood the risk of its decision and "went into 2013 with eyes wide open that the significant price increases planned would inflame [its] customers," and that its aggressive pricing actions would cause an immediate reaction from Novo Nordisk.[250] However, it was seeking to make up for "shortfalls with Lantus demand generation and global profit shortfalls" which it said "put pressure on the US to continue with the price increases to cover gaps."[251] The company conceded that it was "difficult to determine whether we would face these risks anyway if we hadn't taken the price increases."[252]

Internal documents and correspondence show that immediately following Sanofi's 2013 pricing actions, Novo Nordisk increased Levemir's list price in lockstep with Lantus in its continued effort to offer increased rebates and discounts to payers and displace Lantus from preferred formulary placement.

i. In 2014, Novo Nordisk Engaged in Shadow Pricing to Respond to Sanofi's 2013 Pricing Actions

The cornerstone of Novo Nordisk's pricing strategy was to follow Sanofi's actions—a practice that has been referred to as "shadow pricing."[253] Industry observers have described shadow pricing as a phenomenon of "price increases on related brands of aging products from competing companies that often seem to move in synchronized fashion," that "are not tied to the health care inflation rate or cost of goods, but seemingly to the ability of insurance payers and consumers to pay."[254] The practical effect eliminates any meaningful or sustained price variation between Sanofi and Novo Nordisk's basal insulins, which at the time were the only basal insulins available to patients.

Internal documents show that Novo Nordisk's U.S. Pricing Committee (USPC), which makes pricing recommendations for insulin and other drugs, repeatedly suggested matching competitors' pricing for insulin and other products. For example, on May 19, 2014, Novo Nordisk's USPC discussed how to price Levemir in response to Sanofi's 2013 pricing actions.[255] Based on an internal presentation created for this meeting, Novo Nordisk's USPC discussed

[250] SANOFI_SFC_00009132, at SANOFI_SFC_00009135.
[251] SANOFI_SFC_00009132, at SANOFI_SFC_00009135.
[252] SANOFI_SFC_00009132, at SANOFI_SFC_00009135.
[253] An internal presentation revealed that Novo Nordisk amended its pricing strategy on October 21, 2013, to follow Sanofi's marketing, access and profits movements" to "Maximize Brand Value." NNI-FINANCE-001699, at NNI-FINANCE-001701.
[254] Anurag Rathore & Faheem Shereef, *Shadow pricing and the art of profiteering from outdated therapies*, NATURE BIOTECHNOLOGY (2019), https://www.nature.com/articles/s41587-019-0049-7. *See* also Lydia Ramsey Pflanzer, *There's something off about the way insulin prices change*, BUSINESS INSIDER (Sept. 17, 2016), https://www.businessinsider.com/rising-insulin-prices-track-competitors-closely-2016-9.
[255] NNI-FINANCE-0001699. Pricing decisions for drugs marketed and sold by Novo Nordisk in the U.S. are made by its USPC. Between 2014 and 2019, Novo Nordisk's USPC was comprised of 17 members with 4 voting members responsible for insulin pricing. The four voting members responsible for insulin pricing are: Doug Langa, Executive Vice President, North America Operations, and President of Novo Nordisk; Steve Albers, Corporate Vice President, Market Access and Public Affairs; David Moore, Senior Vice President, Commercial; and, Ulrich Ottee, Senior Vice President, Finance and Operations. *See* Letter from Raphael Prober, Counsel, Akin Gump, on Behalf of Novo Nordisk, to Senator Chuck Grassley and Senator Wyden (Mar. 8, 2019); Letter from Raphael Prober, Counsel, Akin Gump, on Behalf of Novo Nordisk, to Senator Chuck Grassley and Senator Wyden (June 28, 2019).

whether it should be a follower in the market, in relation to Sanofi, and considered external factors like press coverage, payer reactions, profits, and performance.[256] In each case, the company's strategic recommendation was to follow Sanofi's pricing moves, rather than lead.[257] Of note, the presentation shows that the USPC considered Levemir's performance, which was ahead of 2014's annual budgeting by $89 million, but that "overall company performance [is] behind."[258] The presentation appears to recommend following Sanofi's pricing actions if the brand's performance is the priority, and to lead if the company's performance is the priority.[259] An excerpt of Novo Nordisk's presentation is shown below.[260]

Changing and challenging 2014 environment

Today's Environment	Considerations	NNI Strategic Recommendation
1 **SANOFI** • Lilly biosimilar 18-month stay • Improving financial performance	Sanofi doesn't need to be as aggressive	FOLLOW
2 **PRESS COVERAGE** • New York Times 4/5 *"Even Small Medical Advances Can Mean Big Jumps in Bills"* • Bloomberg 4/30 *"Drug Prices Defy Gravity, Doubling for Dozens of Products"* • 60 Minutes story late May/June?	Sanofi feeling reputational pressure?	FOLLOW
3 **PAYER PRESSURES** • Basal class reviews – big growth in spend • Rebate pressure and price protection	Two key basal negotiations in progress: CVS July, ESI August	FOLLOW/WAIT
4 **PROFITS AND PERFORMANCE** • Levemir® ARP ahead of AB14 +$89M • But overall company performance behind	Brand versus Company?	Brand focus → **FOLLOW** Company focus → **LEAD?**

In alignment with this strategy, Novo Nordisk's USPC debated potential pricing scenarios based on Sanofi's actions, which they projected with a great deal of specificity. The presentation provided options regarding whether the company should follow Sanofi—and increase list price in July—or lead with a 9.9% increase in August which it considered "optically less aggressive."[261] Based on internal memoranda, it appears that Novo Nordisk's USPC decided to revisit the issue with specific recommendations once Sanofi took action.[262]

Less than two weeks later, on May 30, 2014, Farruq Jafery, Vice President of Pricing, Contract Operations and Reimbursement, emailed Novo Nordisk's USPC to inform them that

[256] NNI-FINANCE-001699, at NNI-FINANCE-001702.
[257] NNI-FINANCE-001699, at NNI-FINANCE-001702.
[258] NNI-FINANCE-001699, at NNI-FINANCE-001702.
[259] NNI-FINANCE-001699, at NNI-FINANCE-001702.
[260] NNI-FINANCE-001699, at NNI-FINANCE-001702.
[261] NNI-FINANCE-001699, at NNI-FINANCE-001703.
[262] NNI-FINANCE-001699, at NNI-FINANCE-001703.

"Sanofi took a price increase on Lantus effective today: 16.1% vial and 9.9% pen."[263] He further wrote that the USPC had "agreed that the best strategy for Levemir is to observe the market and maintain list price parity to competitors."[264] Mr. Jafery then requested that Novo Nordisk's USPC vote "ASAP" to raise the list price of Levemir effective May 31, 2014 (the next day) from $191.28 to $222.08 for vials and from $303.12 to $333.12 for pens.[265] Only a few hours after Sanofi took its list price increase, members of the USPC approved Mr. Jafery's request and Novo Nordisk moved forward with a 16.1% increase on Levemir vial, and a 9.9% increase on Levemir FlexPen and FlexTouch.[266] An excerpt of Mr. Jafery's email is shown below.[267]

Dear Pricing Committee:

Sanofi took a price increase on Lantus effective today: 16.1% vial and 9.9% pen.

Based on our PC discussion on 5/19/2014, we agreed that the best strategy for Levemir® is to observe the market and maintain list price parity to competitors**.

As such, we will be moving forward with a 16.1% increase on Levemir® vial and a 9.9% increase on Levemir® FlexPen® and FlexTouch® effective tomorrow 5/31/2014. This is the approach which minimizes Price Protection impact in 2015 (avoids $13M in incremental PP rebates vs. taking after 6/1/14).

As we need to move immediately to ensure the increase is operationalized in time, please reply back ASAP. We have discussed the impact with Brand and Trade on FlexTouch launch and with Market Access on impact on ongoing negotiations. Although this will generate some pushback from customers, it is believed that this can be managed to mitigate negative impact.

Note that the RE2 forecast assumed 14.9% vial and 9.9% pen, so the ARP upside from this increase is **+$32.3M** vs RE2 and **+$125.9M** vs AB14.

List prices resulting from the proposed increase are shown in the table below:

NDC#	Product Name	Current WAC/pkg	Pct Change	WAC/pkg	Effective Date*
00169-3687-12	Levemir®	$191.28	**16.1%**	**$222.08**	5/31/2014
00169-6438-10	Levemir® FlexTouch®	$303.12	**9.9%**	**$333.12**	5/31/2014
00169-6439-10	Levemir® FlexPen®	$303.12	**9.9%**	**$333.12**	5/31/2014

** or as soon as operationally feasible upon approval.*

*** Prior to taking any price increase, Novo Nordisk undertakes a review of all factors relevant to the price increase to ensure that the increase remains consistent with brand pricing strategy.*

Kind regards,
Farruq

By following Sanofi's actions, Novo Nordisk stood to make an additional $125 million in revenue above its baseline estimates for the year.[268] Mr. Jafery noted that the company's second quarter forecast assumed only a 14.9% price increase for vials. Therefore, by following Sanofi's 16.1% increase, the "ARP [annual revenue projection] upside … is +$32.3M in RE2 and

[263] NNI-FINANCE-001713, at NNI-FINANCE-001714. Based on internal memoranda, Sanofi increased Lantus's list price because Lantus was at WAC parity with Levemir. Sanofi believed that the increase would provide a financial upside and bring vial and pen to WAC parity. SANOFI_SFC_00014580.
[264] NNI-FINANCE-001713, at NNI-FINANCE-001714.
[265] NNI-FINANCE-001713, at NNI-FINANCE-001714.
[266] NNI-FINANCE-001713, at NNI-FINANCE-001714.
[267] NNI-FINANCE-001713, at NNI-FINANCE-001714.
[268] NNI-FINANCE-001713, at NNI-FINANCE-001714.

+$125.9M vs AB14."[269] In the same email chain, one USPC member asks whether Novo Nordisk would "pass on" the price increase to CVS's commercial book of business.[270] Mr. Jafery again signaled that the company would follow Sanofi's lead:

> Since we have heard that Sanofi is <u>not passing</u> this through to CVS <u>Commercial</u>, the recommendation is to follow course and not pass on to their commercial book so as not to disadvantage us in the current negotiations. For their Part D business, we have not heard anything yet to indicate that Sanofi is not passing on. In the event of major pushback on the Part D side, we would need to assess implications and decide whether to pass on or not. By taking this by 6/1, this at least provides us this option.[271]

The back-and-forth between Novo Nordisk officials underscores how closely it was monitoring Sanofi's actions, and appears to mirror the approach laid out in a January 27, 2014 presentation regarding the company's bidding strategy that hinged on CVS's Part D business.[272] Novo Nordisk described its bids for the Part D business as "pivotal," and laid out a game of cat-and-mouse across different accounts in which company officials sought to have Levemir be the only therapeutic option on different PBM formularies.[273] Novo Nordisk recognized that offering "attractive exclusive rebates to large, receptive customers" [274] would "encourage a stronger response from Sanofi."[275] However, Novo Nordisk was willing to take this risk because it would result in "immediate volume and value" for the company and could lead to an exclusive deal for CVS's commercial formulary.[276]

Another series of emails show that Novo Nordisk again shadowed Sanofi's price increase in November 2014, increasing Levemir's list price immediately after Sanofi increased Lantus vials and pens by 11.9%. [277] On the morning of November 7, 2014, Novo Nordisk's USPC learned that Sanofi increased Lantus's list price overnight.[278] (An excerpt of this email is shown below.)[279] And, by the afternoon they were asked to approve the same exact price increase for Levemir, which was approved hours later.[280]

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[269] NNI-FINANCE-001713, at NNI-FINANCE-001714.
[270] NNI-FINANCE-001713.
[271] NNI-FINANCE-001713. Emphasis included in the original.
[272] NNI-FINANCE-001939.
[273] NNI-FINANCE-001939.
[274] NNI-FINANCE-001939, at NNI-FINANCE-001941.
[275] NNI-FINANCE-001939, at NNI-FINANCE-001945.
[276] NNI-FINANCE-001939, at NNI-FINANCE-001945.
[277] NNI-FINANCE-001719-20.
[278] NNI-FINANCE-001719-20.
[279] NNI-FINANCE-001719-20.
[280] NNI-FINANCE-001719-20.

From: RDZI (Rich DeNunzio)
Sent: Friday, November 07, 2014 4:03 PM
To: LAG (Lars Green); JESH (Jesper Hoiland); CLEE (Camille Lee); ANAJ (Andy Ajello); CUOT (Curt Oltmans); PFO (Phil Fornecker)
Cc: SEAP (Sean Phillips); DUGL (Doug Langa); FAJA (Farruq Jafery); KAYE (Karen Yee); BKNO (Bill Knott); BBRT (Bill Breitenbach)
Subject: Approval Requested: Levemir Price increase

Dear Pricing Committee,

As stated earlier this morning, we found out, via Trade, that Lantus has taken an 11.9% increase on both their vial and device and we would follow up with a vote post analysis on the optimal time of the increase.

After analyzing the additional cost of rebates and price protection, based on specific contracting terms, it was determined that it makes better financial sense **(~+$10M benefit)** to wait until after the 45th day of the quarter (11/18 is the first feasible date for the increase) vs increasing price today (effective 11/8). **Therefore, we are asking for your approval to follow their 11.9%** on November 18th** (first feasible increase date post the 15th). Approving this request will have a **benefit to 2014 of ~$25M.**

Please respond with your approval prior to November 13th. Please reach out if you have any questions.

Have a nice weekend,
Rich

*** Prior to taking any price increase, Novo Nordisk undertakes a review of all factors relevant to the price increase to ensure that the increase remains consistent with brand pricing strategy.*

NDC#	Product Name	Current WAC/pkg	Pct Change	WAC/pkg	Effective Date
00169-3687-12	Levemir® 10mL vial	$222.08	11.9%	$248.56	11/18/2014*
00169-6438-10	Levemir® FlexTouch® - 5x3mL	$333.12	11.9%	$372.76	11/18/2014*

** or when operationally feasible upon approval.*

The speed with which Novo Nordisk reacted to Sanofi's price changes is notable. Within 25 minutes after learning of Sanofi's price increase, Rich DeNunzio, Senior Director of Novo Nordisk's Strategic Pricing, emailed Novo Nordisk's USPC to alert them of the change and promise a recommendation the same afternoon after reviewing the financial impact of any move.[281] By late afternoon, Mr. DeNunzio had requested Novo Nordisk's USPC "follow [Sanofi's] 11.9% [list price increase] on November 18th" and vote to increase Levemir's list price, which was promptly approved by Novo Nordisk's chief financial officer for U.S. operations, Lars Green.[282]

ii. In 2015, Novo Nordisk Ended its Shadow Pricing Strategy to Set Up a New Basal Insulin Therapy, Tresiba

After more than a year and a half shadowing Sanofi's insulin pricing, Novo Nordisk adopted a new pricing strategy. According to a series of emails sent in 2015, Novo Nordisk's leadership changed their basal insulin strategy in anticipation of launching Tresiba—Novo Nordisk's second generation basal insulin that was a follow-on product to Levemir. The company wanted to ensure that they set a high basal insulin price floor from which to launch

[281] NNI-FINANCE-001719-20.
[282] NNI-FINANCE-001719. Emphasis included in the original.

Tresiba's initial list price.[283] In order to do so, Novo Nordisk broke with its shadow pricing strategy and increased the price of Levemir, independent of a Lantus increase.

In June 2015, Novo Nordisk officials debated increasing Levemir's price increase in July, to set up Tresiba during negotiations with Express Scripts and CVS Caremark for the 2016 contract year.[284] Doing so would be a departure from following Sanofi. Bill Breitenbach, Vice President of Basal Portfolio Marketing, wrote:[285]

> Good morning,
>
> I spoke with Doug last night about the CVS and ESI 2016 negotiations and it appears they should be completed by the end of June. With that in mind, I recommend we pull forward the Levemir price increase to July 1st. Taking an increase in July 1st will be 7 months since our last and given the timing we can take a leadership position. The sooner we take the increase the better positioned we'll be in the market place and for the potential launch of Tresiba. I see more downsides by waiting until September vs moving now.
>
> Thoughts?
>
> BR,
>
> Bill

Mr. DeNunzio, pushed back, arguing there was little upside "outside of the few months of added revenue."[286] He further added that, by allowing Lantus to lead, Novo Nordisk would be better positioned as they launched Tresiba with "payers still on our side in basal and not fighting Tresiba."[287] An excerpt of this exchange is shown below.[288]

> On Jun 2, 2015, at 8:20 PM, RDZI (Rich DeNunzio) <rdzi@novonordisk.com> wrote:
>
> Thanks Bill.
>
> I'm sure I'm swimming upstream on this one, as it sounds like JESH okay moving, but I would hold until September. Assuming we gain tresiba approval, I think we'll launch at the same price if we take increase in July vs September, so because of that and this isn't aligned to strategy (follow lantus and no sooner than 9 months), i don't see the upside outside of the few months of added revenue. I feel we could be better positioned allowing lantus to lead, let them be the bad guys again, and as we launch tresiba we do so into what could be good situation - open environment and payers still on our side in basal and not fighting tresiba. So potentially short term upside of a few months could hinder longer term opportunity and I think fast access/uptake with tresiba could outweigh '15 gain.

In August 2015, as contract negotiations with CVS Caremark came to a close, the question of leading or following on insulin prices came up again. On August 6, 2015, Mr. DeNunzio—who earlier in the year had advocated for Novo Nordisk getting out ahead of Sanofi on insulin pricing—sent an email to Novo Nordisk's USPC asking if there was any appetite to delay Levemir's next scheduled price increase on August 18, 2015.[289] He further noted that

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[283] *See* NNI-FINANCE-001732.
[284] NNI-FINANCE-001771.
[285] NNI-FINANCE-001771.
[286] NNI-FINANCE-001771.
[287] NNI-FINANCE-001771.
[288] NNI-FINANCE-001771.
[289] NNI-FINANCE-001792, at NNI-FINANCE-001793-94.

"LRS said he would recommend waiting due to [the public relations] risk of leading."[290] ("LRS" appears to stand for Lars Rebien Sorensen, Novo Nordisk's former CEO). Mr. Sorensen's view deviated from other senior executives, including "LAG" (Lars Green, SVP and CFO of Novo Nordisk U.S.) and "JESH" (Jesper Hoiland, President and Executive Vice President U.S.), who were "aligned to take [the price increase] now." [291]

In response to Mr. DeNunzio's email, some Novo Nordisk officials raised concerns that CVS, a major account, would push back on the pricing increase.[292] After several back-and-forth emails—and apparently additional behind-the-scenes discussion—the company struck a compromise on the timing of the price increase that would ultimately move Novo Nordisk to get ahead of Sanofi on insulin pricing. Mr. DeNunzio elaborated:[293]

> Lars informed me today that him and Jesper were having a conversation on Levemir and that they have to "manage their stakeholders", which I'm interpreting as ExecMan. ExecMan agreed to take a Levemir a price increase to set up Tresiba, however they have concerns this far ahead of launch/approval (and they want us to be confident of approval before moving/leading with Levemir).
>
> With this said, Jesper and Lars suggested we take an increase with an 8 in front of it, to appease our internal stakeholders (justification is us showing the market we're not going to take double digit increases here anymore), but still moving on the 18th to hit what's in RE2 and 3. I then informed Lars of CVS issue and PrePC thoughts (minus Doug's).

One senior vice president went along with the decision, but expressed his reservations about moving away from the shadow pricing strategy:[294]

> In the end as I have stated all along, I don't believe that we should be leading with price increases. Again, I understand the rationale (certainly as it impacts next generation products) but I think that it hurts the message that we have been sending to the market and a bit of our credibility with payers.

However, any question about the motivation of moving away from shadow pricing are erased in the final approval request to the USPC. On August 14, 2015—just a few days after requesting their input—Mr. Jafery sent an email to the USPC requesting their final approval to execute an 8.2% price increase on Levemir, effective August 25, 2016. According to Mr. Jafery, "the proposed timing and magnitude is slightly later and lower than what we had previously agreed too, but it balances the concerns of ExecMan while also meeting our strategic objectives which are outlined below."[295] ("ExecMan" refers to Novo Nordisk's "Executive Management" team, which is made up of the company's CEO and his direct reports, which are typically executive vice presidents.) An excerpt of this email is shown below.[296] The USPC agreed to Mr. Jafery's proposal that same day.[297]

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[290] NNI-FINANCE-001792, at NNI-FINANCE-001793-94.
[291] NNI-FINANCE-001792, at NNI-FINANCE-001793-94.
[292] *See* NNI-FINANCE-001792-94.
[293] NNI-FINANCE-001792.
[294] NNI-FINANCE-001792.
[295] NNI-FINANCE-001801-02.
[296] NNI-FINANCE-001801-02.
[297] NNI-FINANCE-001801-02.

Rationale:

Timing is important for executing our Tresiba® premium strategy. With FDA approval anticipated late September (or early October) and "soft launch" in mid-November, we want to ensure a Levemir® price increase sooner rather than later to allow enough time for competition to assess and potentially respond in advance of Tresiba® launch.

- HQ asked us to consider delaying the price increase to as close as possible to Tresiba® launch, however, they ultimately agreed that we should use our best judgment to set up Tresiba® for success.
- From a Levemir® access perspective, we have confirmation that Levemir® will remain on formulary in 2016 at CVS and ESI.
- The price increase is still timed to minimize rebate and price protection impact (many of our contracts have language whereby the rebate and price protection are based on our WAC as of mid-point of the quarter). Note that CVS has pushed back on the timing of our list price increases and demanded changes in contract language which will take effect 1/1/16 to address this. We're finalizing the amendment language which is expected to be signed before 8/25.

Magnitude is within industry norms and is lower than recent history in the basal market.

- It sends a signal to stakeholders that we're cognizant of the public discourse around manufacturer price increases.
- The financial impact to 2015 is negligible given that we have CPP of 8%; downside impact to 2016 is ~$11M (vs. RE2 assumption).

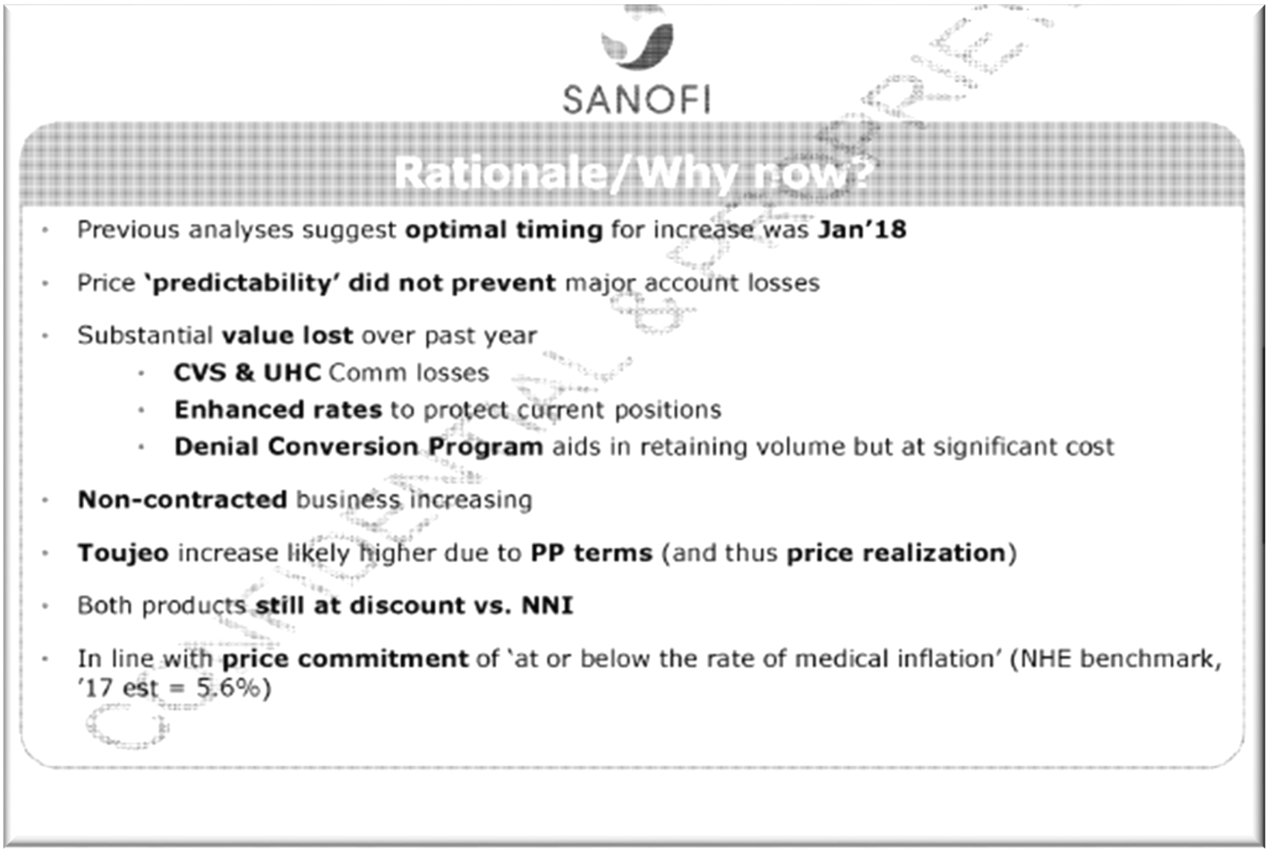
Internal correspondence and memoranda show that Novo Nordisk did not increase Levemir's list price for at least two years following its August 2015 pricing actions and remained the basal pricing leader over Sanofi until 2017. However, Novo Nordisk resumed its strategy of following, rather than leading, Sanofi's pricing actions in 2017 when Sanofi began to increase the price of Lantus.[298]

iii. In 2017 and 2018, Novo Nordisk Resumed Shadow Pricing to Respond to Sanofi's Pricing Actions

Based on data collected for this investigation, Novo Nordisk continued to increase list prices in response to Sanofi's pricing actions. On October 1, 2017, Sanofi increased Lantus's list price by 3% to $256 for vials and $384 for pens, respectively, and Toujeo's list price by 5.4% to $354.[299] Roughly three weeks later, on October 26, 2017, Novo Nordisk's USPC called a "special" USPC meeting to discuss Sanofi's pricing action.[300] During this meeting, Novo Nordisk's USPC debated why Sanofi took a list price increase in October when their "previous analysis suggest optimal timing for increase was Jan'18 [sic]."[301] (An excerpt of the presentation used during this meeting is shown below.)[302] Novo Nordisk believed that Sanofi was forced to pay enhanced rebates and price protection terms to its payer and PBM clients over the past year to protect its current formulary position.[303] In alignment with the list price approach endorsed by its USPC, Novo Nordisk recommended that the company follow Sanofi and take a 4% list price

[298] Internal WAC data shows that Sanofi did not take another list price increase on its long-acting insulins until October 1, 2017. *See* Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, to Senator Grassley and Senator Wyden (Mar. 8, 2019) (attachment 1(a) and (b)).
[299] NNI-FINANCE-003621; NNI-FINANCE-003624, at NNI-FINANCE-003626. *See* Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, to Senator Grassley and Senator Wyden (Mar. 8, 2019) (attachment 1(a) and (b)).
[300] NNI-FINANCE-003621.
[301] NNI-FINANCE-003621; NNI-FINANCE-003624, at NNI-FINANCE-003626.
[302] NNI-FINANCE-003624, at NNI-FINANCE-003626.
[303] NNI-FINANCE-003624.

increase to $279.76 for vials and $419.64 for pens, respectively, in January 2018, which was "approved as recommended on November 3, 2017."[304]

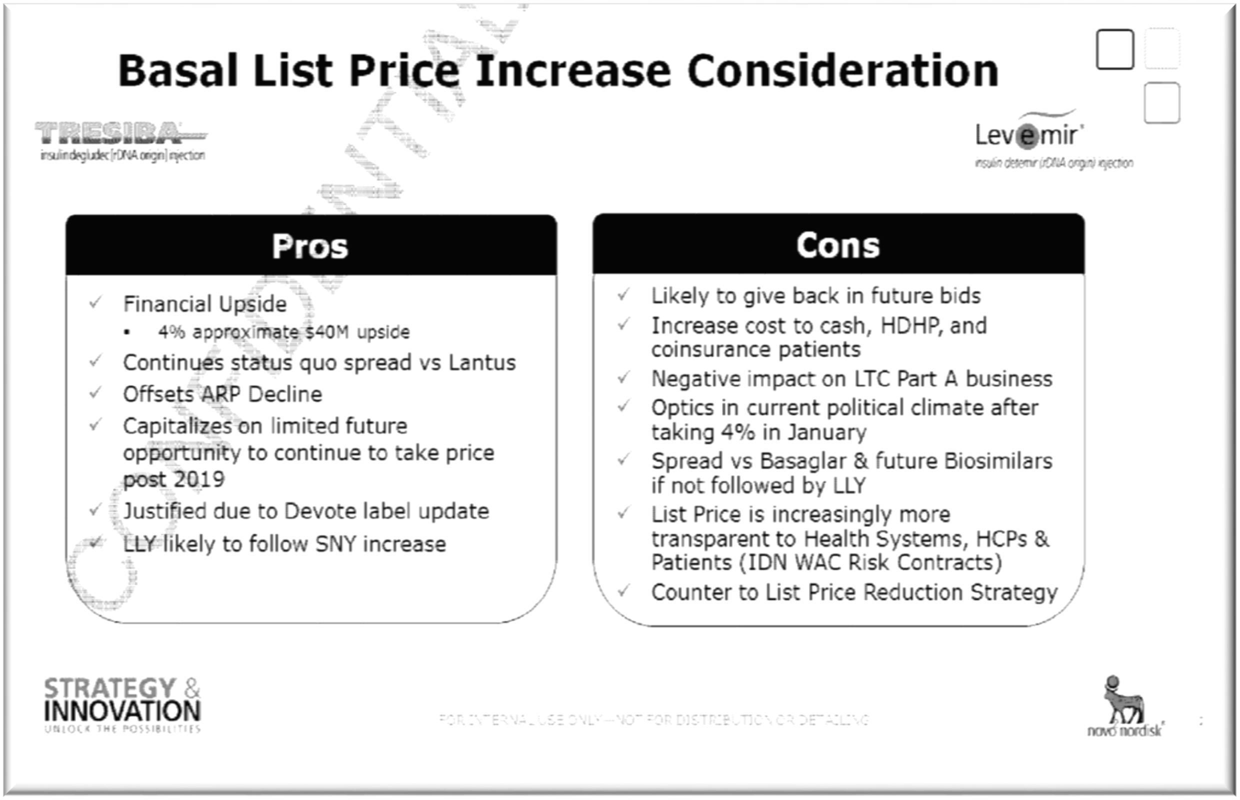


On April 13, 2018, Sanofi again increased the list price of its long-acting insulins by 5.3%, effective May 1, 2018.[305] At this point, the list price of Lantus vials was $269.54 and the price of Lantus pens was $404.29.[306] Based on internal memoranda, it is clear that Novo Nordisk's USPC believed that Sanofi's latest price increase put Levemir at a disadvantage in negotiations with health insurers and their PBMs. On April 19, 2018, Novo Nordisk's USPC recommended another "4% increase on both Levemir and Tresiba."[307]

According to internal memoranda prepared in advance of an April 20, 2018 executive management meeting, Novo Nordisk rationalized its decision with a pro-con list, noting that a 4% increase would result in $40 million gain in revenue and capitalize on "limited opportunities to take price [increases]" with multiple insulin glargine biosimilars on the horizon.[308] The price increase would also stay within Novo Nordisk's commitment to not raise list prices more than 9.9%.[309] This commitment was only taken after the company had spent years dramatically

[304] NNI-FINANCE-000002-03; NNI-FINANCE-003621; NNI-FINANCE-002950.
[305] Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, to Senator Grassley and Senator Wyden (Mar. 8, 2019) (attachment 1(a) and (b)). *See also* NNI-FINANCE-003191, at NNI-FINANCE-003192.
[306] *See* Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, to Senator Grassley and Senator Wyden (Mar. 8, 2019) (attachment 1(a) and (b)).
[307] NNI-FINANCE-003190; NNI-FINANCE-003191-92.
[308] NNI-FINANCE-003190; NNI-FINANCE-003191-92.
[309] NNI-FINANCE-003190; NNI-FINANCE-003191-92.

raising insulin's WAC on which its percentage increases were based. However, the company also noted "cons" which included the increased "cost to cash, [high deductible health plan], and coinsurance patients," a "negative impact on [long-term care] Part A business," and "optics in the current political climate after taking a 4% increase in January."[310] An excerpt of Novo Nordisk's pro-con list is shown below.[311]

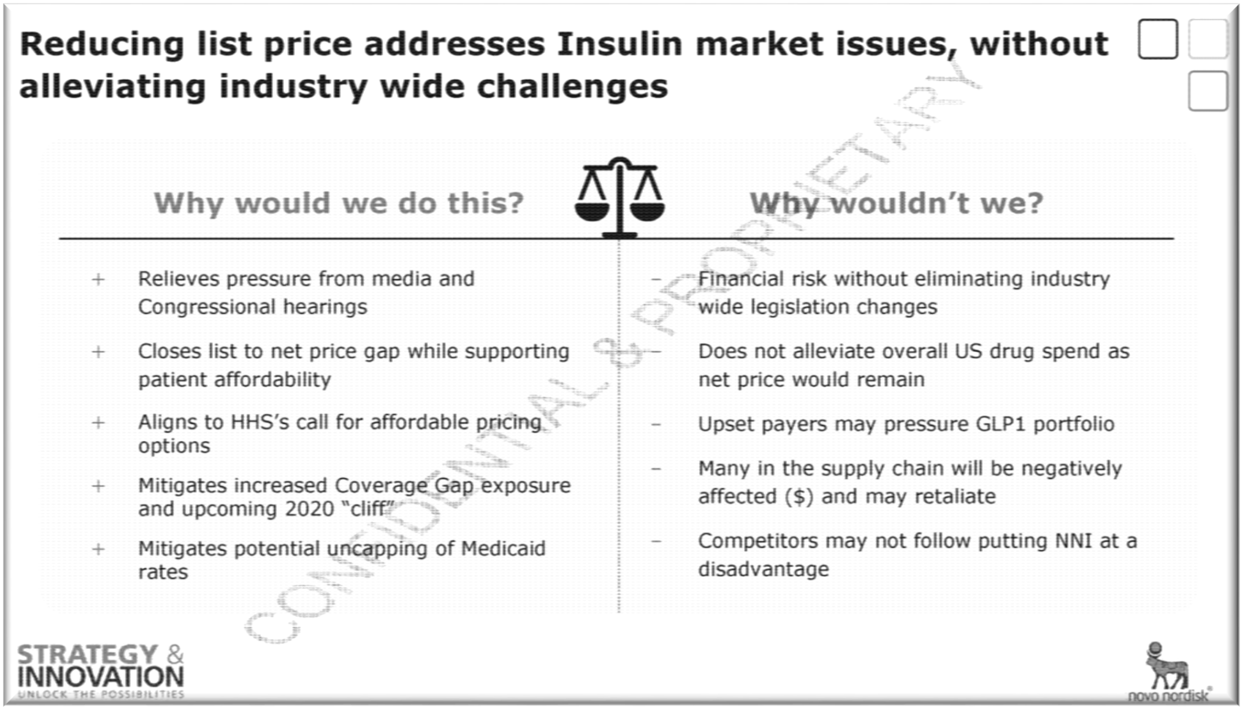


iv. In 2018, Novo Nordisk Discussed List Price Decreases after Feeling Outside Pressure

Following its April 2018 list price increase, Novo Nordisk began to face pressure from payers, the media, and Congress to reduce the price of its insulin drugs.[312] On May 29, 2018, Novo Nordisk's USPC debated whether it should reduce the list price of its insulin drugs by 50% after a string of news reports detailed how patients were struggling to afford their medications.[313] Novo Nordisk believed that a 50% cut would be a meaningful reduction to patients, significantly close the list to net gap, head off negative press attention, and reduce "pressure" from Congressional hearings.[314] However, Novo Nordisk was concerned that a list price reduction

[310] NNI-FINANCE-003190; NNI-FINANCE-003191-92.
[311] NNI-FINANCE-003191.
[312] *See* INSULIN ACCESS AND AFFORDABILITY: THE RISING COST OF TREATMENT, SENATE SPECIAL COMMITTEE ON AGING, 115TH CONG. (2018); Aimee Picchi, *The rising cost of insulin: "Horror stories every day"*, CBS News (May 9, 2018), https://www.cbsnews.com/news/the-rising-cost-of-insulin-horror-stories-every-day/; Irl Hirsh, *Paying the price for insulin*, STAT (May 17, 2018), https://www.statnews.com/2018/05/17/insulin-paying-the-price/.
[313] NNI-FINANCE-002025.
[314] NNI-FINANCE-002025, at NNI-FINANCE-002026-27.

posed significant financial risk to the company.[315] It is noteworthy that the company's primary concerns were retributive action from other entities in the pharmaceutical supply chain, many of which derive payments that are based on a percentage of a drug's WAC price.[316] An excerpt from a memo created for this meeting is show below.[317]



Despite these concerns, internal memoranda suggest that Novo Nordisk was prepared to lower its list price by 2019 or 2020 if its "must haves" were met, which included an agreement from its payer and PBM clients that they would not retaliate against them by changing their formulary placement and would accept lower rebate percentages.[318] It is unclear if Novo Nordisk eventually received an agreement from its payer and PBM clients. However, according to internal memoranda created for Novo Nordisk's USPC, its board of directors voted against this strategy in June 2018 and recommended that the company continue its reactive posture.[319] The rationale for this decision was the "$33 million downside identified (NovoLog only)," "risk of payer backlash or demand for current rebate on new NDC," and "high likelihood of immediate pressure to take similar action on other products."[320] Following the decision by its board of directors, on August 30, 2018, Novo Nordisk decided to continue its strategy to "monitor the market . . . to determine if other major pharma companies are taking list price [increases]."[321] An excerpt from this email is shown below.[322]

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[315] *See* NNI-FINANCE-003737.
[316] NNI-FINANCE-002025, at NNI-FINANCE-002026.
[317] NNI-FINANCE-002025, at NNI-FINANCE-002026.
[318] NNI-FINANCE-002025, at NNI-FINANCE-002029.
[319] NNI-FINANCE-003906; NNI-FINANCE-003907-08.
[320] NNI-FINANCE-003906; NNI-FINANCE-003907-08.
[321] NNI-FINANCE-002969.
[322] NNI-FINANCE-002969.

From:	FAJA (Farruq Jafery)
To:	DUGL (Doug Langa); UCO (Ulrich Christian Otte); SALR (Steve Albers); DDME (David Moore); MPDU (Pia D'Urbano)
CC:	CBLE (Craig Bleifer); BKNO (Bill Knott); RDZI (Rich DeNunzio); FCC (Franco Cognata); EDCI (Ed Cinca); ELIV (Elena Livshina); BLMI (Blandine Lacroix); JTCX (Jack Cox)
Sent:	11/21/2018 5:56:47 PM
Subject:	PC Vote - CA Notification of Planned Price Increase for Victoza & Execution of 2019 Planned Price Increases
Attachments:	2019 List Price Alignment.pptx

Dear Pricing Committee,

Please recall that on Aug 30 PC discussion around 2019 list price, PC concluded on the following:

- Monitor the market in 4Q18 and Jan. 2019 to determine if other major pharma companies are taking list price. If the market supports it, we would continue to take a list price increase in 2019 across our portfolio (with the exception of NovoLog, NovoLog Mix and Novolin)
- Continue to stick to our pricing pledge and do not anchor to another benchmark such as NHE (Nat'l Healthcare Estimate)
- Limit any price increases to once per year <u>per brand</u>

In November 2018, Novo Nordisk learned that Pfizer intended to increase the list price for 41 of its products (or 10% of its portfolio) effective January 15, 2019.[323] Novo Nordisk also discovered that Bristol Myers Squibb and Allergan would do the same in January 2019.[324] After learning of these list price increases, Mr. Jafery immediately emailed Novo Nordisk's USPC and requested a vote to move forward with all "other 2019 planned increases effective February 1 instead of June 2019."[325] Novo Nordisk would ultimately proceed with its 2019 planned list price increases and vote to increase Levemir's and Tresiba's list prices by 4.9%.[326] On January 8, 2019, Levemir cost $308.14 per vial and $462.21 for pens.[327]

e. Beyond Long-Acting Insulin: Companies Used Shadow Pricing Across Multiple Product Lines

Novo Nordisk was not the only company that mimicked its competitor's price increases, nor was the practice limited to long-acting insulins. Documents produced by Eli Lilly and Sanofi show that these companies, at a minimum, closely tracked and responded to price increases. For example, on May 30 2014, company officials at Eli Lilly proposed increasing the list prices of Humalog and Humulin by 9.9%.[328] At the time, the list prices for these drugs were $184.30 per

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[323] NNI-FINANCE-002969.
[324] NNI-FINANCE-002969; NNI-FINANCE-002971.
[325] NNI-FINANCE-002969; NNI-FINANCE-002971.
[326] NNI-FINANCE-003988; NNI-FINANCE-002063. The investigation sought information from insulin manufacturers between 2013 and 2019. Therefore, the Committee cannot determine whether Novo Nordisk continued to follow Sanofi's list price increases in 2020.
[327] NNI-FINANCE-000002-03.
[328] LLY-SFCOM-UR-00003044, at LLY-SFCOM-UR-00003045.

vial for Humalog and $99.80 per vial for Humulin.[329] In asking for a price increase, a company official noted:[330]

From: Michael B Mason
Sent: Friday, May 30, 2014 5:36 PM
To: Enrique A Conterno
Cc: Martin Bott
Subject: Fwd: Humalog and Humulin - list price

Enrique:

As you know we have been discussing a price increase in June. Attached is our proposed price increase.

Let me know if you have any questions.

Mike

P.S. We learned from public sources on Thursday that Novo took a 9.9% price increase across their Insulin portfolio.

Sent from my iPad

Six months later, on November 19, 2014, when Novo Nordisk increased prices again, Eli Lilly's CEO, John Lechleiter, was notified by Enrique Conterno, the head of the company's diabetes unit, who wrote, "[t]oday Novo took a price increase of 9.9% for Novolog and 11.9% for Levemir. As you are aware, we have assumed as part of our business plan a price increase of 9.9% for Humalog before the end of the year."[331] Mr. Conterno, discussing the move with his colleagues over email a few days later, noted, "[g]iven Novo's price increase, let's compensate by taking the price increase earlier,"[332] adding later that day, "I think we should push for [a list price increase] asap given that Novo has taken a price increase already and thus, distributors will start to inventory."[333] Ultimately the company decided to move up their planned pricing increase in response to Novo Nordisk's unexpected price increase, and reiterated that their distributors would expect a price increase from Lilly.[334]

This investigation also showed that Sanofi had a shadow pricing strategy for their short-acting insulin, Apidra, which it called a "fast follower" approach. In November 2014, Sanofi's USPC recommended Sanofi approve a WAC increase of 9.9% because "Apidra has employed a fast follower strategy to Novolog/Humalog prices increases – Novolog just implemented their increase effective November 18th."[335] Along with the pricing recommendation, the USPC

[329] LLY-SFCOM-UR-00003044, at LLY-SFCOM-UR-00003045.
[330] LLY-SFCOM-UR-00003044.
[331] LLY-SFCOM-UR-00003198.
[332] LLY-SFCOM-UR-00003200.
[333] LLY-SFCOM-UR-00003202.
[334] LLY-SFCOM-UR-00003206.
[335] SANOFI_SFC_00014206. This request would result in the WAC price of Apidra vials increasing from $184.85 to $203.15 and Apidra Solostar (pens) from $357.10 to $392.45. *Id.*

included a two-line risk assessment stating matter-of-factly that "[a]ll price increases have the potential to subject the organization to public scrutiny from payers, physicians and patients."[336]

This investigation specifically examined manufacturers' business decisions related to insulin and their contracting practices with PBMs and other plans. While not discussed in this report, the Committee's investigation found that shadow pricing is not limited to the insulin product portfolio.[337]

Shadow pricing practices among pharmaceutical manufacturers are simple: leaders lead and the competitors follow. For a time, Sanofi had the higher price in the basal insulin market with Lantus, so Novo Nordisk followed its competitor's pricing signals with Levemir, deviating slightly from the prices Sanofi settled on. Similarly Novo Nordisk had the highest price in the rapid-acting market, with NovoLog, so they led while Sanofi followed with Apidra and Eli Lilly followed with Humalog.

IV. Rebates, Administrative Fees and Other Common Contract Provisions Related to Insulin WAC and Other Therapies

PBMs have been subject to a great deal of scrutiny for their role in rising drug prices.[338] Although they are the centerpiece of drug pricing negotiations, their practices and business relationships remain largely opaque. As discussed above, the lack of transparency is due in large part to the confidentiality of contractual relationships PBMs have with both health insurers and drug manufacturers, as well as Federal laws barring disclosure of some information related to these negotiations.[339] While the HHS OIG found that this "lack of transparency raises concerns that sponsors may not always have enough information to oversee the services and information provided by PBMs,"[340] the industry continues to fight efforts to bring visibility to its operations.[341] Likewise, PBMs were not fully responsive to the Finance Committee's requests during this investigation, variously failing to timely produce documents, produce all of the requested documents, or produce documents that were fully un-redacted.[342]

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[336] SANOFI_SFC_00014206.

[337] For example, *see* SANOFI_SFC_00014352, at SANOFI-SFC_00014358-59.

[338] Duane Schulthess, *Insulin prices and pharmacy benefit manager rebates: pin the tail on the patient*, STAT (Mar. 19, 2020), https://www.statnews.com/2020/03/19/insulin-prices-pbm-rebates/; Oliver McPherson-Smith and Steve Pociask, *Rx middlemen cost American consumers billions each year*, THE HILL (Jan 27, 2020), https://thehill.com/blogs/congress-blog/health care/480155-rx-middlemen-cost-american-consumers-billions-each-year; Laura Entis, *Why Does Medicine Cost So Much? Here's How Drug Prices Are Set*, TIME (Apr. 19, 2019), https://time.com/5564547/drug-prices-medicine/.

[339] *See, e.g.,* 42 U.S.C. 1396r-8(b)(3)(D)(cross-referenced at 42 U.S.C. 1395w-102(d)(2) and 42 U.S.C. 1396r-8(b)(3)(D)).

[340] DEP'T HEALTH AND HUMAN SERVS., OFF. OF INSPEC. GEN., CONCERNS WITH REBATES IN THE MEDICARE PART D PROGRAM (Mar. 11, 2011), https://oig.hhs.gov/oei/reports/oei-02-08-00050.pdf.

[341] Robert Langreth et al., *The Secret System Middlemen Use to Rake in Millions*, BLOOMBERG (Sept. 11, 2018), https://www.bloomberg.com/graphics/2018-drug-spread-pricing/.

[342] On February 25, 2020, the Committee sent OptumRx and Cigna Corporation letters detailing their failure to produce information and records pertaining to their formulary management committees, and other related information. Press Release, Grassley, Wyden Warn PBM: Cooperate with Insulin Investigation or Face Subpoena (Feb. 26, 2020), https://www.grassley.senate.gov/news/news-releases/grassley-wyden-warn-pbm-cooperate-insulin-investigation-or-face-subpoena. Although CVS Caremark didn't receive a public letter, the Committee did not view the company's production to be fully responsive to the senators' requests for information.

At the same time, industry representatives from both sides have attempted to shift blame for increasing drug prices. In response to the Committee's April 2nd letter, CVS Caremark, Express Scripts, and OptumRx blamed drug manufacturers for increasing insulin prices, arguing that they unilaterally set list prices.[343] Sanofi, Novo Nordisk, and Eli Lilly, on the other hand, blamed PBMs for their demand for ever-higher rebates which has caused them to raise list prices to maintain profitability and patient access.[344] Indeed, PBMs have been accused of "play[ing] drug companies off one another"; "want[ing] juicy rebates"; and "profiting on all sides."[345] What is clear is that the money that flows through PBMs is nothing short of enormous. As discussed throughout this report, rebates have grown at a rapid pace in the insulin market in recent years, which is not true in all therapeutic markets. A 2016 memo to Eli Lilly's executive committee underscored the evolving market:[346]

Executive Committee Executive Summary
2017-2018 Lilly Diabetes Business Plan Review
November 2016

2) US G2N – Given the high level of rebates in diabetes, and especially in the insulin space, the 2017 U.S. G2N liability for diabetes is estimated at nearly $9.2B (on US gross sales of $14B). The Plan incorporates the most contemporary G2N assumption set (including the most current rebate, discount, market share, and segment projections across key Commercial and Part D payers) to estimate this liability, yet even a small percent variance to Plan could result in a material adjustment to reported net sales. The percent contracted and segment mix are assumed to materialize as forecasted as every 1 percent G2N deviation impacts net sales by $100M.

As Congress considers policy solutions to address prescription drug costs, it is important to understand how rebates and other PBM contracting practices contribute to list price increases, especially in the insulin therapeutic class. The following section provides insight into the PBMs' business practices and their role in the insulin market.

a. Rebates for Insulins Have Increased Exponentially Since 2013

343 Letter from Enu Mainigi, Counsel, Williams & Connolly, on Behalf of CVS Health Corp., to Senator Grassley and Senator Wyden (Apr. 26, 2019); Letter from Enu Mainigi, Counsel, Williams & Connolly, on Behalf of CVS Health Corp., to Senator Grassley and Senator Wyden (May 24, 2019); Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, Corporation, to Senator Grassley and Senator Wyden (Apr. 16, 2019); ORX_Sen_Fin_00001935.
344 Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, on Behalf of Sanofi, to Senator Grassley and Senator Wyden (Mar. 8, 2019); Letter from Raphael Prober, Counsel, Akin Gump, on Behalf of Novo Nordisk, to Senator Grassley and Senator Wyden (Mar. 8, 2019); Letter from Joseph Kelly, Vice President, Global Affairs, Eli Lilly, to Senator Grassley and Senator Wyden (Mar. 8, 2019).
345 Duane Schulthess, *Insulin prices and pharmacy benefit manager rebates: pin the tail on the patient*, STAT (Mar. 19, 2020), https://www.statnews.com/2020/03/19/insulin-prices-pbm-rebates/; Oliver McPherson-Smith and Steve Pociask, *Rx middlemen costs American consumers billions each year*, THE HILL (Jan 27, 2020), https://thehill.com/blogs/congress-blog/health care/480155-rx-middlemen-cost-american-consumers-billions-each-year; Laura Entis, *Why Does Medicine Cost So Much? Here's How Drug Prices Are Set*, TIME (Apr. 19, 2019), https://time.com/5564547/drug-prices-medicine/.
346 LLY-SFCOM-UR-00006921.

Based on internal memoranda and correspondence collected for this investigation, the practice of offering rebates in the insulin therapeutic class appears to be contributing to both increasing insulin WAC prices and limited uptake of lower-priced products. Drug manufacturers—typically on an annual, but sometimes more frequent, basis—submit bids to PBMs which reflect a variety of different rebate offers that manufacturers are willing to pay depending on where the drug is placed on a health plan's formulary.[347] However, it's important to note that the final agreement does not guarantee a product's placement. Instead, health insurers make the final decision with regard to formulary placement and the patient's cost-sharing responsibility for the product.

This investigation found that manufacturers offer substantial rebates to PBMs and their clients for the purposes of securing preferred formulary placement for their products, and to ensure strong market access by securing formulary positions that minimize cost-sharing for patients.[348] Low cost-sharing is an important consideration for manufacturers when developing their rebate offers because patients often gravitate towards the cheapest drug to save on their out-of-pocket expenses. A patient's cost-sharing responsibility can affect a manufacturer's market share and profitability.

As noted above, rebates for insulins have increased steadily as manufacturers attempted to secure preferred placement. Rebate offers made by Sanofi and Novo Nordisk to CVS Caremark have increased exponentially between 2013 and 2019. For example, in July 2013, Sanofi offered rebates between 2% and 4% for preferred placement on CVS Caremark's client's commercial formulary.[349] Five years later, in 2018, Sanofi rebates were as high as 56% for preferred formulary placement.[350] Similarly, rebates to Express Scripts and OptumRx increased dramatically between 2013 and 2019 for long-acting insulins. For example, in 2019, Sanofi offered OptumRx rebates up to 79.75%[351] for Lantus for preferred formulary placement on their client's commercial formulary, compared to just 42%[352] in 2015. Similarly, in 2017, Novo Nordisk offered Express Scripts rebates up to 47%[353] for Levemir for preferred formulary placement on their client's commercial formulary, compared to 25%[354] in 2014.

This investigation also found that rebate offers for Medicare Part D, and other high-control formularies, appear to be just as high (if not higher) than those offered for placement on PBMs' commercial formularies. For example, in 2019, Novo Nordisk offered rebates as high as 71% for preferred formulary placement on CVS Caremark's Medicare Part D formulary.[355]

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[347] Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, on Behalf of Sanofi, to Senator Grassley and Senator Wyden (Mar. 8, 2019); Letter from Eni Mainigi, Counsel, CVS Caremark, to Senator Grassley and Senator Wyden (Apr. 26, 2019). Rebates are often calculated on a per unit basis and are billed to the drug manufacturer monthly after the drug is dispensed at the pharmacy. *See* Cigna-SFC-00009847. PBMs also reserve the right to solicit new bids or new offers based on changes in the marketplace, and often do so each year. *Id.*
[348] Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, on Behalf of Sanofi, to Senator Grassley and Senator Wyden (May 24, 2019).
[349] CVSCM_SFC_0003979, at CVSCM_SFC_0004000.
[350] CVSCM_SFC_0004331, at CVSCM_SFC_0004334.
[351] ORX_Sen_Fin_0009384, at ORX_Sen_Fin_0009413.
[352] ORX_Sen_Fin_0009066, at ORX_Sen_Fin_0009078.
[353] Cigna-SFC-00009578, at Cigna-SFC-00009582.
[354] Cigna-SFC-00009535, at Cigna-SFC-00009544.
[355] CVSCM_SFC_0004991, at CVSCM_SFC_0004993-94.

Similarly, in 2019, Eli Lilly also offered rebates as high as 74%[356] for preferred formulary placement.

Rebates have increased for several reasons. Just three PBMs (CVS Caremark, Express Scripts, and OptumRx) now manage 80% of drug benefits for more than 220 million Americans, resulting in manufacturers facing high stakes when negotiating for formulary placement.[357] Pharmaceutical companies are sensitive to the sheer size of PBMs and the resulting product volumes they can affect, which allows the middlemen to extract higher rebates from manufacturers through the use of formulary exclusion tactics. Internal memoranda and correspondence collected for this investigation suggest that manufacturers seek to avoid triggering Medicaid "best price" when developing their bids for commercial plans.[358] As discussed in more detail in this report's background section, under Medicaid "best price," drug manufacturers must give Medicaid the lowest price they offer private plans, wholesalers, providers, and other purchasers, with rebates taken into account.[359] However, rebates offered to Part D plans are excluded from the Medicaid best price calculation, allowing manufacturers to offer higher rebates under Medicare Part D without triggering best price.

Manufacturers have increased their rebates in order to win preferred formulary placement and block competitors. In 2016, Sanofi and Novo Nordisk enhanced their rebate offers around the same time Eli Lilly introduced Basaglar, a follow-on biologic to Lantus. Basaglar is a long-acting insulin and is "[c]linically . . . very similar" to Lantus.[360] Because of its near clinical equivalence, Basaglar introduced additional competition in the long-acting insulin market. Payers used the competition to threaten to switch to Basaglar because it was priced lower and they expected Eli Lilly to offer larger discounts. (This investigation confirmed Eli Lilly offered rebates between 60% and 70% off WAC).[361] A 2016 Sanofi memo describes the market dynamic:[362]

- Lilly is actively engaged with Anthem for 2017 Medicare and commercial business. Anthem believes they would not have significant challenges moving to Basaglar in 2017 if the WAC price and discounts are in line with what they are thinking (20% lower WAC and discounts >40%)

356 CVSCM_SFC_0004838, at CVSCM_SFC_0004843.
357 Letter from Raphael Prober, Counsel, Akin Gump, on Behalf of Novo Nordisk, to Senator Grassley and Senator Wyden (June 28, 2019).
358 *See* SANOFI_SFC_00014281, at SANOFI_SFC_00014285. In developing its OptumRx Medicare Part D bid for Lantus, Sanofi discusses how its pricing strategy for Toujeo could set a high "best price" and thus a high Medicaid rebate "from day one and for the lifecycle of Toujeo." *Id.*
359 42 U.S.C. 1396r-8(c)(1)(C)(i).

> The term 'best price' means, with respect to a single source drug or innovator multiple source drug of a manufacturer (including the lowest price available to any entity for any such drug of a manufacturer that is sold under a new drug application approved under section 505(c) of the Federal, Food, Drug, and Cosmetic Act), the lowest price available from the manufacturer during the rebate period to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or governmental entity . . . *excluding* . . . any prices charged . . . [to] part D."

Id.
360 SANOFI_SFC_00011791.
361 CVSCM_SFC_0004784, at CVSCM_SFC0004805.
362 SANOFI_SFC_00012618, at SANOFI_SFC_00012619.

In an attempt to avoid payers switching to Basaglar, Sanofi and Novo Nordisk increased their rebate bids to respond to Eli Lilly. For example, according to internal memoranda collected from Sanofi, sometime around April 2016, Express Scripts requested bids for its 2017 national commercial formulary and indicated its desire to only add one insulin glargine product to its basal insulin category.[363] Express Scripts communicated to Sanofi that "with the right competitive price, [it] would not have significant challenges moving [from Lantus and Toujeo] to Basaglar"[364] and that Sanofi must enhance its current rebate rate of 42% to maintain current access for their basal insulins.[365] An internal Sanofi memo describes this dynamic:[366]

> **Likely Competitive Approach and Response:**
>
> - Lilly is actively engaged with ESI for 2017 commercial business. Pricing has not been confirmed however ESI has informed that the following assumptions pose a threat to Sanofi's glargine franchise:
>   - Discounts for Basaglar in the mid 60's have been communicated by ESI to Sanofi. This is likely a starter for ESI to consider excluding Lantus and Toujeo. Modeling assumed 70%.
>   - Basaglar WAC will be 15% to 25% less than the WAC price of Lantus. Sanofi modeling assumed 15%.
> - ESI has signaled, with the right competitive price, they would not have significant challenges moving to Basaglar in 2017 despite a follow-on biologic (Basaglar) approval.
> - In addition ESI has indicated that Novo must also enhance its current rate to maintain current access for their basal insulin(s). Novo is likely to enhance its current rebates given recent Tresiba addition to part D formulary.

Rebate contracts confirm that Sanofi increased its offer up to almost 55%[367] off its WAC of $248.51 for Lantus vials and $372.76 for Lantus pens.[368]

i. Rebates Vary Widely by Payer

Rebates also vary greatly across payers. For example, payers with more bargaining power (i.e., more members) enjoy higher rebates than payers with less bargaining power (i.e., fewer members). Although the investigation did not seek out agreements between PBMs and health insurers, manufacturer rebate agreements do support the assertion that smaller health insurers do not always enjoy the same level of rebate offers as their larger peers. For example, in 2014, Novo Nordisk offered WellPoint, the largest for-profit managed health care company with over 40 million members, a larger rebate (40.625%) for Novolin vials for preferred formulary placement as 1 of 2 manufacturers on their client's commercial formulary compared to North Carolina State Employees (27.625%).[369] Similarly, Eli Lilly proposed a widely divergent rebate bid within a

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363 SANOFI_SFC_00012279.
364 SANOFI_SFC_00012279, at SANOFI_SFC_00012280.
365 SANOFI_SFC_00012279, at SANOFI_SFC_00012281.
366 SANOFI_SFC_00012279, at SANOFI_SFC_00012280.
367 Cigna-SFC-00009781, at Cigna-SFC-00009786.
368 Letter from Jeffrey Handwerker, Counsel, Arnold & Porter, on Behalf of Sanofi, to Senator Grassley and Senator Wyden (Mar. 8, 2019) (attachment 1(a) and (b)).
369 Cigna-SFC-00009550, at Cigna-SFC-00009552.

few months of each other for Humulin and Humalog to a commercial health plan in Puerto Rico called SIS (25%),[370] Cigna (45%-55% depending on formulary placement),[371] a PBM called Abarca Health (up to 54%),[372] and Optum's Part D business (68%).[373] A Sanofi presentation for its long-acting insulin products further underscores how rebates can vary not only between companies, but between books of business within those companies, with larger accounts tending to receive larger rebate offers:[374]

Glargine 2018 Tracker

Glargine 2018 Bids

		Lives (M)	Latest Offer Date	Latest Offer Blended Rate	Offer Details	Status	Expected Date of Notification	Term	Offer Gross Sales	Offer Net Sales	Approved Rates Blend	Approved Rates LAN	Approved Rates TOU	2018 LRP Gross Sales	2018 LRP Rate	2018 LRP Net Sales	2018 LRP Access Start Date	2018 LRP Form Position	Δ vs LRP
Commercial	ESI	50.2	06/16/17	69%	1-1 70/70%, 1-2 68/68%, 1-3 63/63% (L/T)	In progress	9/30/2017	1/1/18-12/31/19	1,162	359	63%	65%	60%	1,147	69%	351	1/1/2018	Pref 1of3	8
Commercial	CVS*	41.7	06/16/17	61%	Lantus 1-1 70%, 1-2 68% 1-3 64% Toujeo 1-1 68%, 1-2 65% 1-3 61%	Loss	8/3/2017	1/1/18-12/31/18	101	38	70%	70%	70%	101	66%	34	1/1/2018	NC	3
Commercial	UHC Optum Rx	15.9 10.5	07/15/16	51%	No Opportunity (UHG) Tier 2 = 51% (OPT)	No update from 2017		1/1/17-12/30/20	224	110	65%	65%	65%	224	65%	78	1/1/2018	Pref 1of2	31
Commercial	Humana	2.5	03/20/17	52%	1-1 63% L, 61% T 1-2 53% L, 51% T	In progress	9/30/2017	1/1/18-12/31/19	35	17	55%	55%	53%	35	55%	16	1/1/2018	Pref 1of2	1
Commercial	Aetna	9.6	5/15/17 P 5/16/17 V	54%	Prem 1-2 55% L, 52% T Value 1-2 58% ('18), 62% ('19)	Prem ACCEPTED Value Loss	8/10/2017	1/1/18-12/31/19	81	37	59%	60%	58%	81	58%	34	1/1/2018	Pref 1of2 Val NC	3
Commercial	CIGNA	6.4	05/23/17	0%	1-1 55%, 1-2 51%, 1-3 38%, 55% (T), 6% pp	Loss	6/19/2017	1/1/18-12/31/19	25	25	51%	55%	55%	123	55%	55	1/1/2018	Pref 1of2	(31)
Commercial	Prime	12.5	10/06/16	50%	1-2 50%	No update from 2017	N/A	1/1/17-12/31/18	224	112	54%	57%	52%	224	60%	90	1/1/2018	Pref 1of2	22
Medicare	ESI	4.5	06/01/17	56%	1-1 ESI PDP 63%, 1-1 56%, 1-2 54%, 1-3 53%, 6% PP	In progress	10/1/2017	1/1/18-12/31/19	619	276	55%	56%	54%	619	54%	287	1/1/2018	Pref 1of2	(11)
Medicare	CVS	8.9	08/03/17	78%	Plus/Custom (1-2) LAN 80% LIS/74% STD TOU 75% LIS/69% STD Choice/Template (1-3) LAN 80% LIS/72% STD TOU 75% LIS/67% STD 0% PP LAN, 3% PP TOU	In progress	10/1/2017	1/1/18-12/31/19	1,071	239	64%	65%	60%	1,157	69%	356	1/1/2018	Pref 1of2	(117)
Medicare	Optum Rx	7.8	11/06/16	60%	1-1 66%, 1-2 60%	In progress	8/23/2017 (UHC) 10/1/2017 (Optum)	1/1/18-12/31/19	1,087	430	65%	65%	65%	1,087	64%	391	1/1/2018	Pref 1of2	39
Medicare	Humana	7.5	03/20/17	52%	1-1 63% L, 61% T 1-2 53% L, 51% T	In progress	9/1/2017	1/1/18-12/31/19	720	346	55%	55%	53%	720	52%	346	1/1/2018	Pref 1of2	-
Medicare	Aetna	2.7	12/12/16	69%	Currently NC, 1-2 70% L, 65% T	In progress	10/1/2017	1/1/18-12/31/19	12	4	55%	55%	53%	12	52%	6	1/1/2018	NC	(2)
Medicare	CIGNA	1.4	12/16/16	36%	1-2 36%	In progress	10/1/2017	1/1/18-12/31/19	180	116	39%	39%	39%	180	40%	108	1/1/2018	Pref 1of2	7
Medicare	Prime	1.1	02/14/17	54%	1-1 56%, 1-2 53%	In progress	10/1/2017	1/1/18-12/31/19	125	58	52%	53%	51%	125	54%	58	1/1/2018	Pref 1of2	(0)
	Kaiser	8.1	08/12/16	66%	LAN = 65% TOU NP = 15%, Fixed Price	Status Quo	8/12/2016	1/1/17-12/31/20	139	47	66%			139	66%	48	1/1/2018	Pref 1of1	(0)

SANOFI

USMarket Access

b. PBM Contracting Practices May Contribute to High Rebates and High List Prices in the Insulin Therapeutic Class

In response to the Committee's April 2nd letter, CVS Caremark, Express Scripts, and OptumRx stated that they work to obtain the lowest net cost (the drug price realized by plan sponsors after receiving rebates, discounts, and other fees from manufacturers) by soliciting

[370] LLY-SFCOM-UR-00003596, at LLY-SFCOM-UR-00003597.
[371] LLY-SFCOM-UR-00003325, at LLY-SFCOM-UR-00003326.
[372] LLY-SFCOM-UR-00003532. *See Smarter PBM Platform Selected by PerformRx*, PR Newswire (Oct. 22, 2018), https://www.prnewswire.com/news-releases/abarcas-smarter-pbm-platform-selected-by-performrx-300734745.html. (Abarca is a PBM with a significant customer base in Puerto Rico. It serves more than 2.5 million lives, but is relatively small when compared to CVS Caremark, Express Scripts, and OptumRx.)
[373] LLY-SFCOM-UR-00003449.
[374] SANOFI_SFC_00010668.

manufacturers to submit competing rebate offers.[375] While net cost is an important data point to consider, it does not address WAC, which can affect the price patients pay at the counter. Information collected for this investigation suggests that certain contracting and business practices may create incentives for PBMs to favor drugs with high rebates and, in turn, discourage manufacturers from competing to lower WAC prices.

i. Use of Exclusion Lists

Prior to 2012, most health insurers offered patients open formularies, giving them the ability to access "non-formulary" drugs with higher copays.[376] This changed in 2012 when CVS Caremark began excluding drugs from its formulary and expanded the practice in the following years.[377] Other PBMs and insurers would follow suit,[378] although internal documents show that health plan clients expressed concern about patients being able to access insulin and other prescription medications.[379] Today, the practice is widely used by PBMs, as demonstrated by the roughly 400 medications Express Scripts excludes from its 2021 formularies—an almost eight-fold increase since 2014.[380]

An internal Sanofi memo detailed the company's view on how the ACA changed market dynamics between manufacturers and health plans. The memo also laid out some of the ACA provisions that provided the government additional regulatory power over the private health care market that likely resulted in increased costs to health plans and more restrictive formularies. Portions of the memo and Sanofi's view on how the ACA altered the market dynamics between pharmaceutical companies and payers are listed verbatim below:

- ***Guaranteed Issue/Elimination of Pre-Existing Condition Denials***. *Beginning in 2014, health plans are no longer allowed to deny enrollment or policy enrollment based [on] their costly pre-existing conditions. This increases health plans' costs.*

- ***Elimination of lifetime and annual covered benefit spending.*** *Before the health care law, many health plans set an annual or lifetime limit – a dollar limit on their yearly spending for each enrollee's covered benefits. Enrollee's [sic] would need*

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375 Letter from Enu Mainigi, Counsel, Williams & Connolly, on Behalf of CVS Health Corp., to Senator Grassley and Senator Wyden (Apr. 26, 2019); Letter from Kristin Julason Damato, Vice President Government Affairs, Cigna Corporation, to Senator Grassley and Senator Wyden (Dec. 7, 2020); ORX_Sen_Fin_00001935.
376 SANOFI_SFC_00009132. *See also* Joshua Cohen et al., *Rising Drug Costs Drives the Growth of Pharmacy Benefit Managers Exclusion Lists: Are Exclusion Decisions Value-Based?*, HEALTH SERV. RES. (Aug. 2018), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6056588/.
377 SANOFI_SFC_00009132, at SANOFI_SFC_00009134.
378 SANOFI_SFC_00009132, at SANOFI_SFC_00009134.
379 A series of internal memos outlined health plans' concerns about Express Scripts' decision to begin excluding drugs from their national formulary. Some clients threatened to terminate their relationship with the PBM. Cigna-SFC-00015251. Another client's insurance board ruled it could not "adopt this strategy … due to their union contract obligations and their diabetes education funded by Novolog." Cigna-SFC-00015246. Other clients raised concerns related to disruption to their beneficiaries, such as "increased costs due to additional office visits and additional member hassle." Cigna-SFC-00015242. And, "major member disruption." Cigna-SFC-00015244. *See* Cigna-SFC-00015236-60.
380 In 2014, Express Scripts excluded approximately 57 drugs from its formulary. In 2021, that figure jumped to over 400. *See 2021 National Perferred Formulary Exclusion Lists*, EXPRESS SCRIPTS (2021), https://www.express-scripts.com/art/open_enrollment/DrugListExclusionsAndAlternatives.pdf.

to pay for the medical expenses beyond those limits. ACA no longer allows plans to do this. This increases health plan's [sic] costs.

- ***Medical loss ratio.*** *Health plans must meet certain thresholds when it comes to revenue and expenses. The intent of the MLR is to eliminate excess profits and encourage administrative efficiencies. Plans must demonstrate that at least 80% of their revenues (85% in the large group market) must be accounted for with enrollee medical expenses. If they do not, consumers must receive rebate checks to bring the accounting into line with the threshold. The US government has publicized that in 2012, consumers received $500 million in MLR rebate checks and avoided $3.4 billion in upfront premium increases that would have occurred had this and other polices not been in place. This is money that has been taken out of the health care plan sector.*

- ***Government premium rate reviews.*** *Health plans must submit to the government justification for any premium rate increases of 10% or greater. The US government has publicized that in 2012, consumers saved $1.2 billion as a result of this policy. This is money that has been taken out of the health plan sector.*

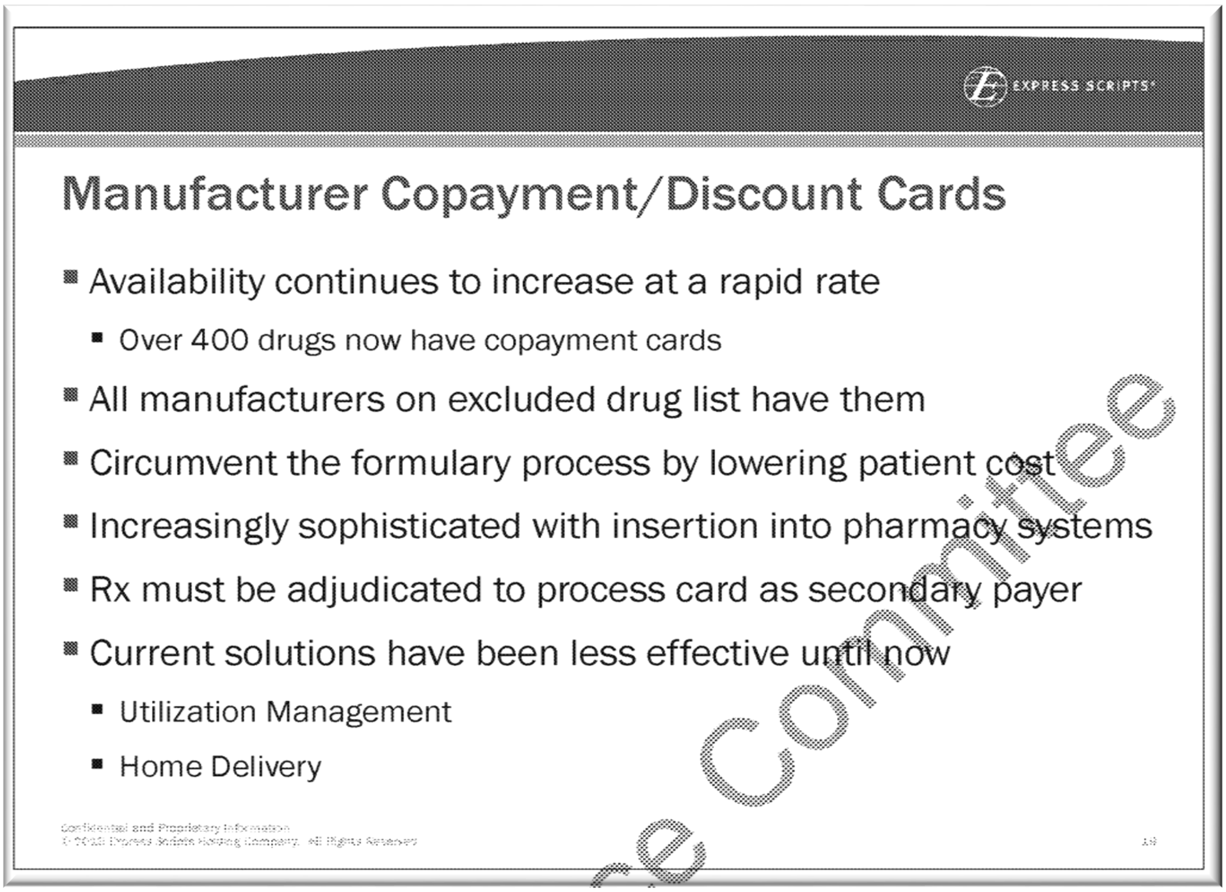
- ***Fees to support the exchanges****. In order to manage some of the risk of high cost enrollee's [sic] in the exchanges, health fees have been imposed on plans outside of the exchanges. Additionally, for health plans that participate in the exchanges, fees are imposed for participation. This increases plan's [sic] costs. The 10 essential health benefits. The ACA requires plans to cover 10 essential health benefits: 1) ambulatory patient services; 2) emergency services; 3) hospitalization; 4) maternity and newborn care; 5) mental health and substance use disorder services, including behavioral health treatment; 6) prescription drugs; 7) rehabilitative services and devices; 8) laboratory services; 9) preventive and wellness services and chronic disease management; and 10) pediatric services, including oral and vision care. For those plans that did not offer such robust benefits previously, their costs increased with ACA . . .*

- ***Uncertainty on enrollment and patient mix.*** *Exchange plans are expected to cover the medical expenses of a currently uninsured population. No historical data exists as to whether or not the consumer penalties associated with not buying insurance (the individual mandate) is significant enough to encourage enrollment of healthy individuals. In the event health plans end up covering only the sick, and those expenses exceed the revenue generated from premiums, plans will incur losses. While there are risk protections in place to help compensate for some of these risks and losses, much uncertainly [sic] still exists.*

- ***[Formulary coverage policy.]*** *Finally, the ACA set a precedent with is formulary coverage policy. While this policy does not place pressure on plan's [sic] margins, it does provide an excuse for health plans to assert more exclusivity on drug formularies. ACA regulation allows plans to cover one drug per USP category. (Medicare requires at least two drugs per category). Plans may choose to exploit*

this precedent setting government policy as they operate in the non-exchange market in order to leverage more rebates and reduce costs.[381]

Increased use of manufacturer co-payment and discount cards also made it difficult to control drug spending. An internal Express Scripts presentation underscores the PBM industry's view that co-pay coupons circumvent the formulary process by lowering patient costs and incentivizing patients to use drugs with higher list prices.[382] An excerpt concerning manufacturer copay coupons taken from an Express Scripts internal memo is shown below.[383]



When a drug is excluded from a formulary it means that it will not be covered by the insurer unless an exception is granted for the patient.[384] In the insulin therapeutic class, PBMs consider certain insulins interchangeable, meaning that their P&T committees have determined the competing brands are similar in their safety, efficacy, and kinetics.[385] The P&T's determination allows PBMs to solicit competing bids from manufacturers in an effort to obtain

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[381] SANOFI_SFC_00009132, at SANOFI_SFC_00009132-33.
[382] Cigna-SFC-00018522, at Cigna-SFC-00018540-41.
[383] Cigna-SFC-00018522, at Cigna-SFC-00018540.
[384] Letter from Michael Bopp, Counsel, Gibson Dunn, on Behalf of Cigna Corporation, to Senator Grassley and Senator Wyden (Apr. 16, 2019).
[385] *Id. See also* ORX_Sen_Fin_0004777 (OptumRx's P&T had designated Basaglar, Lantus, Levemir, and Toujeo as part of an "essential class"); ORX_Sen_Fin_0005377, at ORX_Sen_Fin_0005383 (Drugs designated as an "essential class" are similar in their safety and efficacy when used to treat the same or similar medical condition).

the lowest net cost for their clients. While formulary exclusions are intended help control drug costs, they can affect a patient's ability to access medication, and revenue generated by drug manufacturers from their products.[386] For the patient, if a drug is excluded, they can be forced to either switch to another product, which could affect adherence and health outcomes, or pay significantly more to stay on their preferred medication. For manufacturers, the investigation found that the mere threat of exclusion typically forces them to offer substantially greater discounts to maintain formulary position, reducing net price. When exclusions are actually imposed, manufacturers often face a significant loss of market share, leading to lower revenue. On the other hand, being the exclusive therapy on a formulary can be advantageous for a brand's market share and revenue, which incentivizes companies to offer large discounts to maintain such status.[387] The use of exclusions has led to a market dynamic in which manufacturers offer ever-higher rebates to avoid exclusion, which appears to have contributed to higher list prices.

The investigation found several instances where manufacturers increased their rebate bids following the threat of formulary exclusion.

Prior to 2013, Sanofi offered an average rebate of 5% on Lantus.[388] However, in 2013, Sanofi began to increase its rebate and discount offerings to health plans for two reasons. First, Sanofi increased its rebate and discount offerings to respond to Novo Nordisk's aggressive rebate strategy.[389] Beginning in 2013, competitors sought to "[d]isplace Lantus in High Control Plans and Markets (i.e., Part D) through increased rebates" for the purposes of capturing market share.[390] Secondly, Sanofi increased its rebate and discount offerings because payers began to demand increased discounts from drug manufacturers to remain on their formulary.[391] A Sanofi memo, shown below, further explains this dynamic:[392]

[386] Letter from Raphael Prober, Counsel, Akin Gump, on Behalf of Novo Nordisk, to Senator Grassley and Senator Wyden (June 28, 2019).
[387] *See* LLY-SFCOM-UR-00003699. This June 2015 email exchange amongst Eli Lilly employees shows how manufacturers seek to maintain exclusive status for their drugs and will offer increased rebates to maintain preferred status.
[388] SANOFI_SFC_00008916-17.
[389] SANOFI_SFC_00014532, at SANOFI_SFC_00014533.
[390] SANOFI_SFC_00009211, at SANOFI_SFC_0009217.
[391] SANOFI_SFC_00009211, at SANOFI_SFC_0009217.
[392] SANOFI_SFC_00009211, at SANOFI_SFC_0009217.

MARKET OVERVIEW
Lantus

- Aggressive Competitors
  - Displace Lantus in High Control Plans and Markets (i.e. Part D) through increased rebates and/or portfolio offers for the sole purpose of removing Lantus from favorable formulary access
  - Attempts to minimize the clinical differentiation between Lantus and Levemir
- Aggressive Payers
  - Price Predictability
    - Accounts requiring more value from price predictability
      - Extension of Timeline/WAC Evaluation periods lengthened, e.g. Caremark Price Protection from June 2013 thru December 2014 for the 2014 Contract, ESI Requesting 2-Year Price Protection
      - Demand for lower threshold percentages
      - Discontinue calculations that exclude prior pricing activity from carrying forward, e.g. no more Reset Calculations
  - Increased Discounts
    - Caremark increase in base rebates was needed to remain on formulary
      - Caremark Base 25% to 32% for 2014
  - Benefit Designs
    - Accounts have shown willingness and ability to remove Lantus from Formulary
    - Cigna 2012, Aetna 2013, OptumRx Saver Plus 2013, Coventry 2014

While PBMs may have initially utilized formulary exclusions in the insulin therapeutic class as a way to drive cost down for their clients, internal correspondence and memoranda suggest that increased use of formulary exclusions have had unintended consequences: WAC prices have continued to increase, leading to higher prices for some at the pharmacy counter.

For example, in 2013, Express Scripts threatened to move patients to other diabetes drugs in order to "break even on [the] rebate line" unless Sanofi increased its Medicare Part D rebate offer for Lantus in 2014.[393] As a result, Sanofi considered increasing its rebate offer from 7.45% to 15% in order to prevent formulary exclusion.[394] Sanofi also faced similar pressure to increase rebates for Express Scripts' commercial contracts. Internal memoranda collected from Sanofi suggest that "Sanofi was notified by [Express Scripts] that Lantus was positioned to be removed from the formulary effective 2013 . . . [as a result] rebates were re-negotiated."[395] An excerpt from this memo, discussing the threat to Lantus, is shown below.[396]

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[393] SANOFI_SFC_00009282, at SANOFI_SFC_00009287-88.
[394] SANOFI_SFC_00009282, at SANOFI_SFC_00009287.
[395] SANOFI_SFC_00008920, at SANOFI_SFC_00008923.
[396] SANOFI_SFC_00008920, at SANOFI_SFC_00008923.

Lantus Contracting History with ESI
Account Management and Contracting have worked closely together to maintain a 5% rebate for Commercial contracts through 2012. Sanofi was notified by ESI that Lantus was positioned to be removed from formulary effective 2013. Rebates were re-negotiated resulting in a 6% Lantus Vial & 9% Lantus SoloStar rebate (no price protection).

Lantus Overall Threat
The Commercial business is at additional threat due to competitive rebate pressures and changing formulary design as well as Lantus pricing actions.

- ESI has shared that Novo has been extremely aggressive the last few months and this has triggered the need to revise our offer.
  - For 2014 ESI made Humalog exclusive in the RAI category, moving Novolog to Not Covered and made Byetta & Bydureon the only options in the GLP1 category, moving Victoza to Not Covered.
- Comments during discussion with ESI confirmed that modeling has occurred and that the current contracted offer will result in a Not Covered position for 2015. This is based on competitive offers by Novo and client plans requesting exclusive offers for comparison.
- They have shared that the basal category is under consideration for exclusion list status for 2015. This interest in an exclusive offer is consistent with recent actions they have taken to reduce the number of branded options available to patients.
- Lantus price increases over the past two years have positioned Sanofi as a cost driver that has triggered significant attention from ESI.

Express Scripts is an important account to retain for Sanofi's diabetes drugs because of the large volume of its customer base. According to internal memoranda, in 2014, Express Scripts and its affiliated businesses managed the prescription drug claims of over 4.6 million people, representing 15% of the total business in the Medicare Part D channel.[397] Rebate agreements confirm Sanofi renegotiated rebates and entered into an agreement to provide up to 10.625% for Lantus, effective January 1, 2014.[398] Rebates were renegotiated again that same year, and Sanofi increased its rebate offer up to 14.625%, effective October 1, 2014.[399]

Around this same time, payers eventually learned that Sanofi had offered competitive rebates to Express Scripts which caused them to question their rebate status with Lantus.[400] As a result, payers began to demand higher rebates and threatened to exclude Lantus from their formulary to achieve this result. For example, in 2014, UnitedHealthcare (UHC) threatened to remove Lantus from its commercial formulary because of Lantus's price increases.[401] Sanofi offered an enhanced rebate for FY2015 in the 15% range, but UHC rejected Sanofi's offer and removed Lantus from its commercial formulary.[402] Sanofi responded with a last minute bid of 45% rebate for Tier 2 which UHC countered with 45% for Tier 3.[403] According to Sanofi, UHC's counteroffer was "ultimately accepted over access concerns to future products and the need to secure access to patient lives."[404] Rebate agreements confirm Sanofi renegotiated rebates

[397] SANOFI_SFC_00009282, at SANOFI_SFC_00009283.
[398] Cigna-SFC-00010029, at Cigna-SFC-00010040.
[399] Cigna-SFC-00010043, at Cigna-SFC-00010044.
[400] For example, in 2014, internal memoranda suggest that Sanofi was "at risk with [Prime Therapeutics] due to public comments around increases in Lantus rebates impacting the U.S. market for diabetes." According to Sanofi, at the time, "Prime is questioning their current rebate status with Lantus . . . [and] are requesting/requiring an increase in 2015." SANOFI_SFC_00014267.
[401] SANOFI_SFC_00008934.
[402] SANOFI_SFC_00008934.
[403] SANOFI_SFC_00008934.
[404] SANOFI_SFC_00008934. Emphasis included in the original.

and entered into an agreement to provide up to 45% for Lantus, effective December 15, 2015.[405] An excerpt of this email exchange is shown below.[406]

From: Ingram, Garrett PH/US
Sent: Tuesday, August 19, 2014 4:12 PM
To: Guenter, Peter PH/FR; Purcell, Andrew PH/US; Bartner, Natalie PH/US; Whitaker, Anne PH/US; Kaseta, Michael PH/US
Cc: Du, Wei Wei PH/FR; Bray, Scott PH/US; Borneman, James PH/US; Loreaux, Sandy PH/US; McClellan, Mike PH/US
Subject: RE: Lantus Weekly Report - Week Ending August 1, 2014

Andrew, Peter & all,

Per Andrew's response the contract is performing to the expectations/forecasts we set when we signed the deal. We will continue to monitor and focus on accelerating pull through. Below is our initial assessment. Additionally, attached are the whitepapers & financials for the OptumRx Commercial & Part D deals. Due to the sequence of events we have completed a post action review that we will be sharing with you in September. Our response to customer feedback resulted in incremental impact. Look forward to reviewing learnings with you. Please let me know if you have any questions or feedback. Best,

Garrett

UHC Commercial and Part D Response

Overview: Driven by increasing costs in the basal category, including sanofi price increases on Lantus, UHC approached sanofi with a request for incremental commercial rebate targets. Following a series of sanofi offers in the 15% range, UHC removed Lantus from commercial formulary. Sanofi responded with a last minute bid of 45% for Tier 2 which was rejected by UHC who counteroffered with a 45% rebate for Tier 3 + 7% cumulative PP. Although this offer was deemed to be negative financially vs. a no-contract scenario, the offer was ultimately accepted over access concerns to future products and the need to secure access to patient lives.

In Part D, UHC similarly moved to remove Lantus from formulary in 2015, particularly unhappy about the December 2013 pricing action and suggesting that agreed terms of 35% +7% PP were insufficient. Final terms of 55% + 6% PP were agreed to which also included access to the Saver Plus formulary, a segment of lives of which Lantus had previously been excluded. Lantus Vial added - 7/1/14 and SoloSTAR -10/1/14.

Similarly, in 2016, Express Scripts threatened to remove Lantus and Toujeo from its Medicare Part D formulary and requested that Sanofi submit its "best and final offer" or else face formulary exclusion.[407] According to internal memoranda, during negotiations, Express Scripts told Sanofi that it was justified in removing Lantus and Toujeo from its Medicare Part D formulary because it had allowed "quite a few years of price increases" and that Novo Nordisk's rebate offer was more competitive.[408] In response to Express Scripts' threat, Sanofi discussed revising its rebate offer up to 40% with 4% price protection for Lantus and Toujeo.[409]

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405 ORX_Sen_Fin_0009099, at ORX_Sen_Fin_0009126.
406 SANOFI_SFC_00008934.
407 SANOFI_SFC_00012556, at SANOFI_SFC_00012558.
408 SANOFI_SFC_00012556, at SANOFI_SFC_00012558.
409 SANOFI_SFC_00012556.

Although contracts with PBMs included larger and larger rebates, manufacturers still expected to remain profitable—up to a point. For example, on July 28, 2017, one Sanofi official wrote to colleagues after considering their offer to CVS Caremark for placement on the Part D formulary: "After inclusion of additional fees, we are still profitable up to an 89% rebate."[410] The official included an analysis that assumed "CVS would need to shift 68.9% of [its] glargine volume to Novo to break even (at an assumed 81% rebate offer)."[411] In its analysis, Sanofi compared various negotiation scenarios including a "no contract" scenario, which it determined would be more profitable to the company even with the resulting reduction in sales volume and revenue.[412] It appears that one of the deciding factors was optics, as one colleague put bluntly: "How would it look to be removed from the largest Medicare plan?"[413]

As PBMs expanded the practice of using exclusions to extract greater rebates, Sanofi's counterstrategy was to bundle unrelated products that had been excluded—Lantus and an epinephrine injection called Auvi-Q—to win formulary inclusion for both. (Bundling is a practice where manufacturers offer rebates and discounts for multiple products, but only if certain conditions are met.) Both drugs had been excluded from various accounts, such as some of Aetna's Part D plans, resulting in rapid erosion of market share:[414]

Background:

- As of 3Q14, Aetna has approximately 2.3 Million Medicare Part D lives (~6% of MMA channel) in the U.S.
- Aetna acquired Coventry in May 2013 and enhanced Medicare footprint by adding > 1.0 Million Part D members with largest enrollment in Texas, Michigan, California and Pennsylvania.
- Lantus is in a Not Covered position for 60% of the business and Non-Preferred for 40% of the business.
- Lantus Family market share share fell from 66.3% (1/13) to 47.3% (1/14) and is currently 33.7% (9/14). Lantus was moved to Not Covered on Aetna's MMA formulary on 1/1/13.
- Auvi-Q is in a Not Covered position for 100% of the business and market share is 0.6% (9/14).

Sanofi faced significant financial pressure across all accounts, and sought to include bundling agreements in several of its contracts. While negotiating contracts for the 2015/2016 plan year, Express Scripts advised Sanofi that they needed to be far more aggressive with rebate offers to gain access to the PBM's commercial book of business than in past years.[415] Internally, Sanofi officials warned in a memo that "Novo, specifically Levemir, has changed the game with regard to rebates," and that Sanofi would "need to rebate aggressively."[416] The memo noted that Lantus and Auvi-Q were initially bundled together—an offer that had since been withdrawn from consideration.[417] A separate presentation describes "[c]ontracts that increase Lantus rebates if Auvi-Q is added to [the] formulary thus creating a bundled arrangement," and notes that the company had even considered a "triple product bundle" with Toujeo, despite concerns about the

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410 SANOFI_SFC_00010874.
411 *Id. See also* SANOFI_SFC_00010880, at SANOFI_SFC_00010884.
412 SANOFI_SFC_00010874, at SANOFI_SFC_00010877-79; SANOFI_SFC_00010880, at SANOFI_SFC_00010883.
413 SANOFI_SFC_00010874.
414 SANOFI_SFC_00013990.
415 SANOFI_SFC_00014648.
416 SANOFI_SFC_00014648.
417 SANOFI_SFC_00014648, at SANOFI_SFC_00014653.

arrangements triggering Medicaid best price.[418] It's important to note that this counterstrategy was not limited to Sanofi. Another internal memo shows that Sanofi's competitors were using the same strategy: "Lantus is losing accounts and share within the institutional channel because of aggressive discounting and bundled contract offerings from Novo Nordisk and Lilly."[419]

Sanofi was not the only company that sought to use bundling to its advantage. For example, Novo Nordisk secured contract terms from CVS's Part D business in 2013 that tied its "exclusive" rebates for insulin to formulary access for a Type 2 diabetes drug called Victoza. The exclusive rebates of 57.5% for Novolin, Novolog, and Novolog Mix 70/30 were more than three times higher than the 18% rebate for plans that included two insulin products on their formulary.[420] In order to qualify for the exclusive rebate, the plans would also need to list Victoza, a GLP-1 agonist,[421] on their formulary, exclude all competing insulin products, and ensure "existing patients using a [c]ompeting [p]roduct may not be grandfathered."[422] CVS also appears to have been prohibited from rebidding for products within the therapeutic class for placement on the national formulary until January 1, 2015, absent safety issues with one of the drugs.[423]

Following years of rebate and list price increases, manufacturers faced increased pressure from patients, payers, and the Federal government to decrease insulin's WAC price.[424] However, internal memoranda and correspondence collected for this investigation suggest that the downstream impact of lowering the WAC prices presented hurdles for pharmaceutical companies. A June 23, 2018 email memorializes a portion of a conversation Eli Lilly's President of the Diabetes Unit, Enrique Conterno, had with the CEO of OptumRx who allegedly "re-stated that [OptumRx] would be fully supportive of Lilly pursuing a lower list price option", but indicated that OptumRx would encounter challenges, namely, "the difficulty of persuading many of their customers to update contracts without offering a lower net cost to them."[425] In response, one executive noted, "we wouldn't be able to lower our list price without impacting our net price," and counseled waiting until early 2020 to reduce prices.[426] Two weeks prior to this email, Eli Lilly executives raised the possibility that PBMs would object to a list price reset because it would result in (1) a reduction in administrative fees for PBMs, (2) a reduction in rebates, which would impact PBMs' ability to satisfy rebate guarantees with some clients, and (3) impair their clients' ability to lower premiums for patients, thereby impacting their market competitiveness.[427] An excerpt of this email is shown below.[428]

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[418] SANOFI_SFC_00013800, at SANOFI_SFC_00013801.
[419] SANOFI_SFC_00009001, at SANOFI_SFC_00009002.
[420] NNI-FINANCE-000039, at NNI-FINANCE-000051.
[421] *GLP-1 agonists: Diabetes drugs and weight loss*, MAYO CLINIC, https://www.mayoclinic.org/diseases-conditions/type-2-diabetes/expert-answers/byetta/faq-20057955 (last viewed Jan 1, 2020).
[422] NNI-FINANCE-000039, at NNI-FINANCE-000052.
[423] NNI-FINANCE-000039, at NNI-FINANCE-000052.
[424] *See* LLY-SFCOM-UR-00005526.
[425] LLY-SFCOM-UR-00006684.
[426] LLY-SFCOM-UR-00006684.
[427] LLY-SFCOM-UR-00006563.
[428] LLY-SFCOM-UR-00006563.

Message

From: Terrence M Lyons [redacted]
Sent: 6/14/2018 2:56:33 PM
To: Enrique A Conterno [redacted]
CC: Frank D Cunningham [redacted] Michael B Mason [redacted]; Joshua L Smiley [redacted]
Subject: Reply: Tomorrow

Enrique:

I anticipate that the PBMs may raise the following objections and/or considerations in connection with a contemplated list price reset:

(1) Reduction in the absolute amount of Admin Fees earned upon insulin claims/utilization (since this is expressed as a percentage) while still performing comparable/identical services governed by the Admin Fee;
(2) Reduction in absolute rebate amounts pressuring the PBMs ability to satisfy contractually obligated rebate guarantees with some clients (employers and insurance plans) in the near/intermediate term;
(3) Inability to modify/resubmit premiums and associated formularies for Part D plans for the 2018 (and perhaps 2019) plan year(s), or risk that such adjustments may impair market competitiveness (i.e rebate levels on lower gross price levels translating to higher plan premiums).

TML

Terrence M. Lyons
Vice President Finance | CFO Lilly Diabetes
[redacted]

The internal memoranda and correspondence collected for this investigation show that exclusion lists have contributed to higher rebates in the insulin therapeutic class. Manufacturers increase rebates to respond to formulary exclusion threats, and to preserve revenue and market share through patient access. It also appears that increases in rebates are associated with increased list prices. This supports the notion that PBM demands for rebates contribute to rising insulin prices.

ii. Administrative Fees

Eli Lilly's reluctance to lower the list price of drugs—due partly to its effect on PBM revenue from administrative fees—illustrates a dynamic that the HHS OIG has identified as an area of concern for potential violations of the Anti-Kickback Statute.[429] According to rebate agreements collected for this investigation, PBMs earn administrative fees for each unit of a manufacturer's drug.[430] These fees, which are negotiated between the manufacturer and PBM in

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[429] *See* DEP'T HEALTH AND HUMAN SERVS., OFF. OF INSPEC. GEN., FRAUD AND ABUSE; REMOVAL OF SAFE HARBOR PROTECTION FOR REBATES INVOLVING PRESCRIPTION PHARMACEUTICALS AND CREATION OF NEW SAFE HARBOR FOR PROTECTION FOR CERTAIN POINT-OF-SALE REDUCTIONS IN PRICE ON PRESCRIPTION PHARMACEUTICALS AND CERTAIN PHARMACY BENEFIT MANGER SERVICE FEES (Feb. 6, 2019), https://www.federalregister.gov/documents/2019/02/06/2019-01026/fraud-and-abuse-removal-of-safe-harbor-protection-for-rebates-involving-prescription-pharmaceuticals. According to the HHS OIG, if administrative fees are tied to the list price of a prescription pharmaceutical product, based on sales volume, or far exceed fair market value of the services performed, these fees could function as a kickback. *Id.* HHS OIG proposed creating a new safe harbor that would provide a pathway, specific to PBMs, to protect remuneration in the form of flat service fees. *Id.*
[430] *See* ORX_Sen_Fin_0009384, at ORX_Sen_Fin_0009389. It's important to note that administrative fees only meant to be applied to drugs utilized by commercial and Medicare Part D plans. These are not charged on products utilized by Medicaid or the Children's Health Insurance Program (CHIP). *Id.*

rebate contracts, are meant to cover services such as reporting and monitoring health insurers' compliance with the rebate eligibility requirements, examples of which are detailed in a rebate contract between CVS Caremark and Novo Nordisk:[431]

(h) Administrative Services. In consideration of the Administrative Fees, PBM will: (i) negotiate and contract with Part D Plan Sponsors for participation in the Rebates provided under this Agreement; (ii) notify Part D Plan Sponsors of the applicable requirements for receiving Rebates on Products in accordance with PBM's standard business practices; (iii) monitor Part D Plan Sponsor compliance with the Rebate eligibility requirements; (iv) calculate the amounts of Rebates applicable to Products for each Part D Plan Sponsor and invoice Manufacturer for such Rebates; (v) prepare detailed reports on Product utilization and Rebate calculations as described herein; (vi) allocate and distribute Rebates to Part D Plan Sponsors under the terms of PBM's agreements with Part D Plan Sponsors and provide supporting reports to the Part D Plan Sponsors; (vii) utilize internal control measures to protect against payment of unearned Rebates; and (viii) provide such other services related to the administration of the Rebate program as agreed upon by the parties from time to time. Administrative Fees are separate and apart from the Rebates paid to Part D Plans.

Administrative fees paid by drug manufacturers are calculated as a percentage off WAC.[432] Some Part D contracts even require manufacturers to pay administrative fees during the coverage gap phase (the phase that occurs between the initial coverage limit and the catastrophic coverage phase) of Medicare Part D.[433]

Although Part D plans are required to report rebates to CMS, they are not required to report administrative fees collected and retained by PBMs "if the fees are for bona fide services and are at fair market value."[434] This basic lack of transparency in the Medicare program has been an area of concern to HHS OIG, as has the competing interests that PBMs and manufacturers find themselves in due to the administrative fees being based on the WAC price. According to HHS OIG:

> When PBMs contract to administer the pharmacy benefit for health plans, the PBMs are the health plans' agents. However, the contracting health plans may not always know the services their PBMs are providing to pharmaceutical manufacturers. Manufacturers often pay PBMs fees for certain services (e.g., utilization management, medical education, medication monitoring, data management, etc.), and these fees may be calculated as a percentage of the list price of a particular drug product. If service fees paid by manufacturers are tied to the list price of the prescription pharmaceutical product, based on sales volume, or far exceed the fair market value of the services performed, these fees could function as a disguised kickback.[435]

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[431] CVSCM_SFC_0005005, at CVSCM_SFC_0005009.
[432] CVSCM_SFC_0005005, at CVSCM_SFC_0005018. *See also* ORX_Sen_Fin_0009384, at ORX_Sen_Fin_0009389.
[433] *See* CVSCM_SFC_0005005, at CVSCM_SFC_0005010.
[434] DEP'T HEALTH AND HUMAN SERVS., OFF. OF INSPEC. GEN., CONCERNS WITH REBATES IN THE MEDICARE PART D PROGRAM, at 4 fn. 16 (Mar. 11, 2011), https://oig.hhs.gov/oei/reports/oei-02-08-00050.pdf.
[435] *See* DEP'T HEALTH AND HUMAN SERVS., OFF. OF INSPEC. GEN., FRAUD AND ABUSE; REMOVAL OF SAFE HARBOR PROTECTION FOR REBATES INVOLVING PRESCRIPTION PHARMACEUTICALS AND CREATION OF NEW SAFE HARBOR FOR PROTECTION FOR CERTAIN POINT-OF-SALE REDUCTIONS IN PRICE ON PRESCRIPTION PHARMACEUTICALS AND

The amount of administrative fees paid industry-wide is not known because they are contained in the confidential rebate contracts with manufacturers and are not disclosed by the PBMs. However, a recent study by the *Pew Charitable Trusts* estimated that, between 2012 and 2016, the amount of administrative and other fees nearly tripled, reaching more than $16 billion.[436] While such totals are far from inconsequential, they appear to make up a relatively small amount of the $370 billion spent on retail prescription drugs in the United States,[437] and make up a relatively small share of the cost of individual pharmaceutical products.[438]

Administrative fees vary by contract, but generally fall between 3% and 5% in the insulin therapeutic class. For example, in 2019, OptumRx's administrative fee for Lantus represented 4.75% of WAC.[439] However, documents collected during the investigation show that PBMs have been collecting substantially greater revenue from administrative fees as WAC prices increase and the fees grow:[440]

Rationale for Recommendation:

- The recommendation is in response to the customer's request to increase Admin Fees from 3.00% to 4.75%.
- Factors leading to the reassessment and increase include:
    - Alignment with market competitive rates
        - Prime Therapeutics → 3%, Caremark →4% ESI →4.875% *note that ESI rate increased in 2016 by .5points*
    - Request of manufacturers to provide increased transparency to client-level compliance with rebate eligibility from prior levels
    - Increased number of manufacturer requested audits
    - Increased complexity of manufacturer required conditions for rebate eligibility
- The incremental 1.75% is <u>not</u> negotiable. If we do not agree to the 1.75% it will be captured from product(s) base rebate.

While the Committee's investigation did not request documents related to the agreement between PBMs and health insurers, Express Scripts provided a *pro forma* contract between the State of Tennessee and Cigna Corporation which suggests PBMs also charge health insurers non-rebate, administrative fees for providing pharmacy benefit management service—essentially profiting from all sides of the transaction.[441] This contract provides that Express Scripts earns administrative fees and, depending on the agreement, clinical fees[442] from the State of

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CERTAIN PHARMACY BENEFIT MANGER SERVICE FEES (Feb. 6, 2019), https://www.federalregister.gov/documents/2019/02/06/2019-01026/fraud-and-abuse-removal-of-safe-harbor-protection-for-rebates-involving-prescription-pharmaceuticals.

[436] *The Prescription Drug Landscape Explored*, Pew Charitable Trust, at 35 (Mar. 2019), https://www.pewtrusts.org/-/media/assets/2019/03/the_prescription_drug_landscape-explored.pdf.

[437] *National Health Expenditures 2018 Highlights*, CTRS. FOR MEDICARE AND MEDICAID SERV. (2018), https://www.cms.gov/files/document/highlights.pdf

[438] *See Prescription Economics in the U.S. Drug Channel System*, DRUG CHANNEL INSTITUTE (Aug. 2017), http://www.drugchannelsinstitute.com/files/Drug_Channel_Economics-Pembroke-August2017.pdf.

[439] ORX_Sen_Fin_0009384, at ORX_Sen_Fin_0009389.

[440] *See* SANOFI_SFC_00012321.

[441] Cigna-SFC-00017902, at Cigna-SFC-00017903.

[442] Clinical fees are defined as the amount paid to the PBM for their management of clinical programs such as safety and monitoring review, prior authorization, and step therapy edits and prior authorization and appeals. Cigna-SFC-00017902, at Cigna-SFC-00017904.

Tennessee, calculated as an agreed upon percentage multiplied by the number of participating members per month.[443] An excerpt from Express Scripts' pro forma contract is shown below.[444]

> a. **Administrative Fee** – The fee for pharmacy benefit management services paid by the State to the Contractor. The Administrative Fee is the only compensation due the Contractor under the contract, unless the Contractor also bid a Clinical Fee. The Contractor's monthly compensation is a function of the contractor's Administrative Fee multiplied by the number of participating Members per month ("PMPM"). The State recognizes that Clinical Fees are not included in the Administrative Fee The State also recognizes that the Contractor may make a margin on mail and Specialty Drugs that it dispenses out of its own pharmacies.

The use of administrative fees between plans and PBMs is further supported by correspondence between Express Scripts and the Securities and Exchange Commission in 2017. The company explained that administrative fees and the percentage of rebates delivered to the plan are both negotiating levers PBMs use with their plan clients:

> The pricing for our PBM offering depends upon the benefit design selected by each individual client. The overall pricing in our client contracts depends on several components, including ingredient costs, administrative fees and rebates. We customize the economics of each client contract based on the client's assessment of how it can cost effectively deliver the pharmacy benefit package that provides appropriate care and value to its members. For example, one client may prefer to keep a greater percentage of rebates and compensate us for our services through greater administrative fees, while another client may prefer to keep a smaller percentage of rebates in exchange for reduced administrative fees. Furthermore, client pricing varies based on the mix of prescriptions dispensed — specifically the type of drug and the distribution method by which the drug is dispensed.[445]

Finally, it is noteworthy that industry observers have suggested that the recent partnership between Express Scripts and Prime Therapeutics may serve as a vehicle to avoid increasing legislative and regulatory scrutiny related to administrative fees by channeling such fees through a Swiss-based group purchasing organization (GPO), Ascent Health.[446] While there are several regulatory and legislative efforts underway to prohibit manufacturers from paying administrative fees to PBMs, there is no such effort to change the GPO safe harbor rules.[447] New arrangements used by PBMs to collect fees should be an area of continued investigative interest for Congress.

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[443] Cigna-SFC-00017902, at Cigna-SFC-00017903.
[444] Cigna-SFC-00017902, at Cigna-SFC-00017903.
[445] *Express Scripts Response to Staff of the U.S. Securities Exchange Committee*, SEC (June 26, 2017), https://www.sec.gov/Archives/edgar/data/0001532063/000119312517213574/filename1.htm
[446] *See* Adam, Fein, *Express Scripts + Prime Therapeutics: Our Takeaways From This Market Changing Deal*, DRUG CHANNELS (Jan. 7, 2020), https://www.drugchannels.net/2020/01/express-scripts-prime-therapeutics-our.html.
[447] *Id.* It's important to note that GPOs are also compensated via manufacturer-paid administrative fees. *Id.*

iii. Price Protection Clauses

In addition to rebates and administrative fees, PBMs also negotiate a price protection provision in their contract such that when a drug company increases the list price of its drug beyond a certain agreed upon percentage, the plan receives an additional rebate.[448] The caps in price protection terms vary widely. For example, one contract amendment between OptumRx and Sanofi had "price protection factors" that allowed the manufacturer to implement annual price increases from as little as 0% to as much as 12% depending on the therapy.[449]An example of a price protection clause in a rebate agreement between CVS Caremark and Sanofi is shown below:[450]

> H. **Additional Rebate for Cumulative Price Protection.** If the WAC of any NDC of a Product listed on a Plan Formulary on a Preferred Brand Tier or Specialty Tier is increased regardless of whether such increase occurs, after the Baseline WAC Date or prior to or after the start of the then current Calendar Year, such that it exceeds the Price Increase Limitation Price for that Calendar Year, then Manufacturer shall pay an Additional Rebate (which shall be in addition to the Base Rebates described above) for that Calendar Year. For purposes of this Section, the following definitions shall apply.

Another CVS contract with Novo Nordisk shows how price protection clauses can also be tied to a drug's net price (i.e. a manufacturer's revenue after rebates and discounts), as it was with Levemir, Novolog, and Novolog Mix 70/30:[451]

> An example of the foregoing adjustment is as follows: If the Baseline WAC for a particular Product is $100, the Rebate Percentage is ten percent (10%), and the Baseline Net Price for the Product is $90, the Net Price Ceiling would be $97.20. If the WAC for such Product increases by $10, the Net Price for the Product would be $99, which exceeds the Net Price Ceiling. The Rebate Percentage would thus increase to 11.64% ($110 - $97.20 = $12.80; $12.80/$110 = 11.64%) in order to maintain a Net Price equal to the Net Price Ceiling.

Such payments are intended to limit annual inflation of a drug's price, and require manufacturers that exceed the cap to pay an additional rebate. An internal presentation from Express Scripts suggests that a portion of these payments may be retained by the PBM.[452] Shown below.[453]

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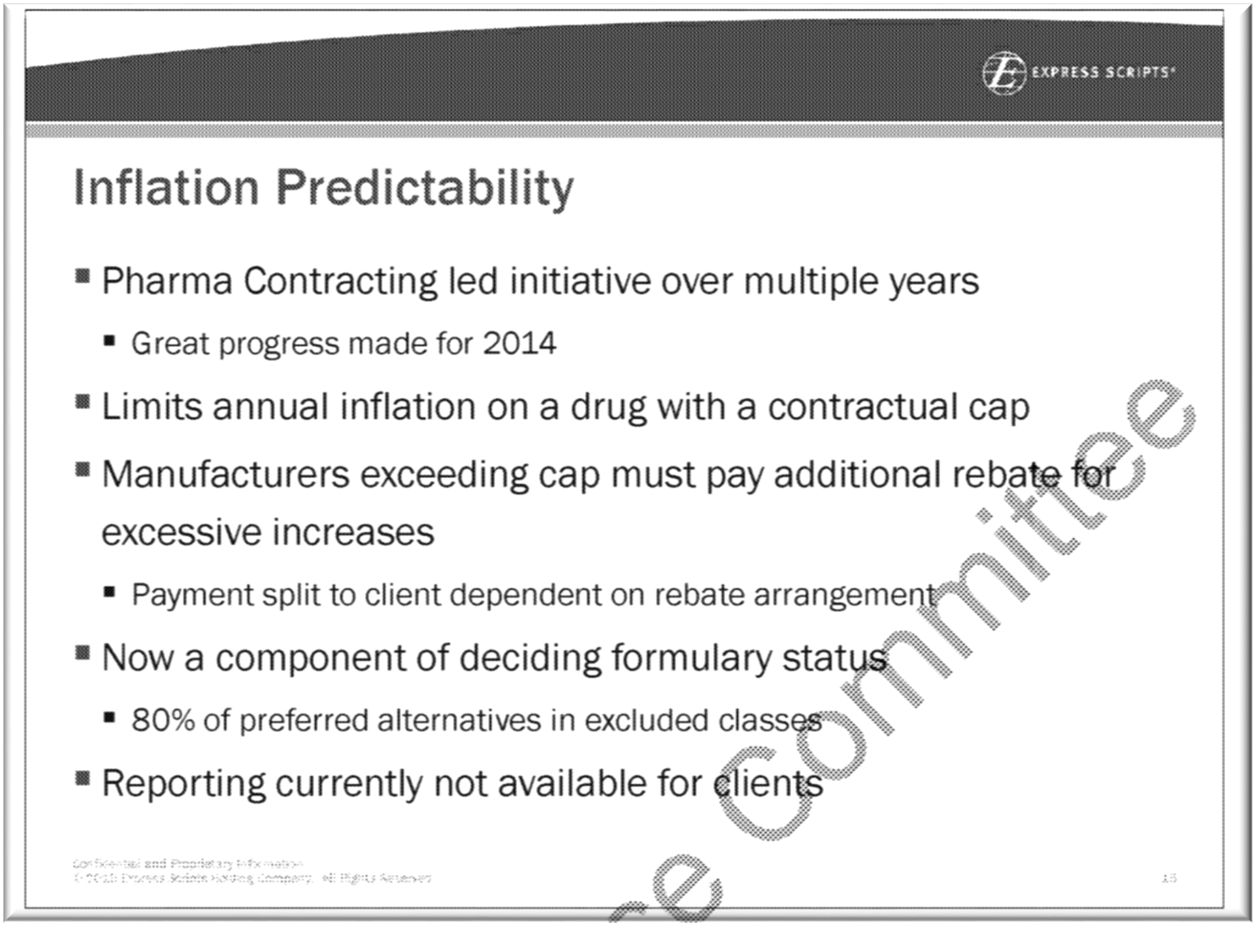
448 *See* CVSCM_SFC_0004331, at CVSCM_SFC_0004356.
449 ORX_Sen_Fin_0009384. Please note that the Committee has redacted non-insulin therapies from this document.
450 CVSCM_SFC_0004331, at CVSCM_SFC_0004356.
451 NNI-FINANCE-000039, at NNI-FINANCE-000052-53
452 Cigna-SFC-00018522, at Cigna-SFC-00018536.
453 Cigna-SFC-00018522, at Cigna-SFC-00018536.



Although price protection clauses are intended to deter manufacturers from increasing prices too quickly, the investigation identified examples of manufacturers who found ways around them. For example, Novo Nordisk avoided price protection payments and rebate payments by timing drug price increases to occur just before or just after price protection penalties would have been triggered. In so doing, the company dodged millions of dollars in penalties for exceeding the contractual ceiling prices.

For example, in October 2014, company employees requested approval to increase the price of NovoLog and Novolin, noting that the “price increase is timed for mid-quarter to minimize price protection impact,” and estimated that the moves would result in a $6 million upside for the brands that year.[454] A later email showed a similar strategy, as Novo Nordisk avoided $25 million in rebates and price protection penalties for Levemir by simply following Sanofi’s price increase. Sanofi had taken a price increase of 11.9% on Lantus vials and pens the night before,[455] and Novo Nordisk employees saw an opportunity to avoid price protection by quickly following suit:

> Please note that many of our contracts look at the WAC price on the 45th day of the quarter (and monthly paid contracts at the 15th day), so … we will determine if it

[454] NNI-FINANCE-001715.
[455] NNI-FINANCE-001719-20.

makes better financial sense (due to rebate payments and price protection) to align the increase to the same date as NovoLog® (11/18).[456]

Following the analysis, the employee recommended that the company wait in order to capture a multi-million-dollar financial benefit:[457]

After analyzing the additional cost of rebates and price protection, based on specific contracting terms, it was determined that it makes better financial sense **(~+$10M benefit)** to wait until after the 45th day of the quarter (11/18 is the first feasible date for the increase) vs increasing price today (effective 11/8). **Therefore, we are asking for your approval to follow their 11.9%** ** **on November 18th** (first feasible increase date post the 15th). Approving this request will have a **benefit to 2014 of ~$25M.**

Novo Nordisk capitalized on this opportunity, making it an integral part of their pricing strategy. The company even built these avoided rebates and penalties into their revenue forecasts. In an email from May 2015, the Pricing Committee was asked to approve a planned price increase to specifically avoid price protection clauses for NovoLog and NovoLin:[458]

We have secured Brand alignment on the timing and magnitude of the proposed increases. Please note that the price increase is timed for just after mid-quarter to minimize rebate and price protection impact. *(Many contracts base the rebate calculation on the WAC in effect at the 45th day of the quarter so taking on May 19 minimizes rebate impact in 2Q).*

Novo Nordisk repeatedly targeted CVS Caremark's Part D contract provisions to avoid paying price protection penalties. By increasing drug prices days before the price protection clauses took effect, Novo Nordisk avoided paying CVS Caremark millions of dollars in payments. In May 2014, the Pricing Committee was asked to approve the prices of NovoLog by the 27th of the month or "sooner to minimize the impact of price protection."[459] By increasing the list price by this date, Novo Nordisk estimated it would avoid paying roughly $12 million in price protection rebates.[460] Indeed, the contract between the two companies shows that the "Baseline Net Price," which the price protection caps are based on, is defined as the "Net Price in effect as of June 1st of the prior Contract Year and Baseline WAC means WAC in effect as of June 1st of the prior Contract Year."[461] This contract further defines the price protection provisions:

> The Net Price for each Product's Formulary Status shall be reviewed monthly by comparing the Net Price of the applicable calendar month to the Baseline Net Price. If the Product's Net Price has been increased by more than eight percent (8.00%) over Baseline Net Price ("Net Price Ceiling"), the Rebate percentage(s) for such product will be increased for such calendar month such that the Net Price will equal the Net Price Ceiling. The increased Rebate percentage(s) shall remain in effect during the remainder of the current Contract Year and shall return to their original percentage at the beginning of the next Contract Year.[462]

[456] NNI-FINANCE-001719-18
[457] NNI-FINANCE-001719.
[458] NNI-FINANCE-001766.
[459] NNI-FINANCE-001709.
[460] NNI-FINANCE-001709.
[461] NNI-FINANCE-000082.
[462] NNI-FINANCE-000082, at NNI-FINANCE-000086.

The Pricing Committee approved the request and increased NovoLog and Novolin on May 28, 2014, three days before the 2015 CVS Caremark Part D pricing protection went into effect.[463] Two days later, Novo Nordisk took another price increase aimed at CVS Caremark Part D's 2015 price protection loophole, this time with its basal insulin, Levemir. Contract Operations Vice President Farruq Jafery informed the Pricing Committee that Sanofi had increased the price of Lantus—16.1% for the vial and 9.9% for the pen[464]—and that Novo Nordisk should follow their actions. He recommended Novo Nordisk follow Sanofi's lead and swiftly institute an identical pricing change (as discussed in further detail above) to avoid $13 million in incremental price protection rebates.[465]

However, by the time the 2016 contract bid cycle started in August 2015, CVS Caremark had caught on to Novo Nordisk's strategy and began to push back against Novo Nordisk's practices related to price protection:[466]

> **Background on CVS:**
>
> We know CVS has stated their disappointment with our price increase strategy (ie: taking just after the 45th day) and how it essentially results in a lower price protection, admin fee and rebate payment for that quarter/time after our increase. I don't think there's any disputing how we operationalize our price and that we do it this way to create the most value to NNI, but it has been costing CVS a good amount of money.
>
> When CVS was here last week they reiterated their concern and Farruq/Brenda have committed to working on solution (WAC as of dispensed date), to be operationalized in 2016 with a resolution from a financial perspective to be effective 1/1/16 (ie: if implemented in 7/1/16 they will receive adjustment for the 1st half of 2016). CVS is requesting this to go back to 7/1/15.

To appease CVS, Novo Nordisk considered delaying a price increase on Levemir, but as the increase "capitalize[d] on all contracts" the company questioned the financial implications of such a move:

> We're scheduled to take a Levemir price increase next week (8/18) and Karen is about to finalize the formal email to [the] PC. The 18th is the first day after the 45th day we could operationalize the increase. We're doing it to capitalize on all contracts (rebate and PP payments). Specifically with CVS Maria is estimating that it will result in about $3.8M favorably to NNI (on the flipside cost CVS $3.8M then if they had WAC as of dispensed). Our price increase on **Levemir roughly garners us $2.5M per week and it costs CVS about $634k, so financially it makes sense to take the increase by about $2M per week. Question: Is there any appetite to delay the increase by a week or two so it's not apparent to CVS or are we okay recommending to PC as planned?**[467]

Despite their concerns with CVS, Novo Nordisk would approve the increase just after the 45th day of the quarter, even as the pricing committee agreed that CVS would "be upset regardless."[468] However, Novo Nordisk was not the only insulin manufacturer that repeatedly

463 NNI-FINANCE-001965.
464 NNI-FINANCE-001711, at NNI-FINANCE-001712.
465 NNI-FINANCE-001711, at NNI-FINANCE-001712.
466 NNI-FINANCE-001792, at NNI-FINANCE-001793.
467 NNI-FINANCE-001792, at NNI-FINANCE-001793-94. Emphasis added.
468 NNI-FINANCE-001792.

sought to avoid price protections. Eli Lilly internal communications also cited the elimination of price protection penalties as a reason for price increase timing.[469] These examples suggest that payers and PBMs accept list price increases as long as the increases do not affect their ability to collect higher rebates and discounts from manufacturers. However, this approach can lead to higher prices for the Federal government and individual consumer.

V. Conclusion

Diabetes is one of the most pervasive and deadly diseases in the United States. Millions of Americans live with this disease, and millions more are expected to be diagnosed this year alone. This disease also disproportionately impacts minority communities, rural communities, and those who are 65 and older. As insulin's list price has grown over time, so too have costs to consumers and the Federal government. As a result of these price increases, some diabetic patients have reportedly resorted to rationing their insulin medication, putting their lives at risk. Rising drug costs have also further strained the U.S. health care system.

The Committee conducted this investigation to better understand how the list price of insulin, a drug that's been available to patients for almost a century, has doubled (and, in some cases tripled) over the past decade. In pursuit of the facts, the Committee requested and reviewed over 100,000 pages of internal documents, memoranda, and rebate agreements produced by the three largest insulin manufacturers (Sanofi, Novo Nordisk, and Eli Lilly) and the three largest PBMs (CVS Caremark, Express Scripts, and OptumRx) in the United States. While the Committee feels that it received sufficient information to support the findings in this report, it notes that Novo Nordisk, CVS Caremark, Express Scripts, and OptumRx failed to fully respond to the Committee's document requests.

The investigation underscores how the opaque business practices of pharmaceutical manufacturers and PBMs have huge implications for patients, payers, and the Federal government, with respect to insulin and therapies for other diseases.

Insulin manufacturers compete fiercely, using rebates as bargaining chips to receive preferred formulary placement for their products and to block competition. The companies undertake these bidding wars to maximize revenue and capture—or maintain—market share. Furthermore, in some cases the investigation found that while insulin manufacturers closely monitor their competitors' pricing actions when determining their own list prices over time, there were multiple instances of companies <u>increasing</u> prices in lockstep with competitors. In part, insulin manufacturers make those decisions due to countervailing pressures in their relationships with PBMs. Higher list price increases the dollar value of rebates, discounts, and other fees that a manufacturer can offer to a PBM and health plans, which are based on a percentage of the list price. Internal documents showed that insulin manufacturers were sensitive not only to their own bottom lines, but the bottom line of PBMs and of health plans that set formularies, without which a manufacturer's product would likely lose significant market share.

PBMs appeared to be complicit in this behavior. There appeared to be little, if any, attempt by PBMs to discourage manufacturers from increasing the list price of their products. Instead, the Committee found that PBMs used their size and aggressive negotiating tactics, such as the threat of excluding drugs from formularies, to extract more generous rebates, discounts,

[469] LLY-SFCOM-UR-00003202, at LLY-SFCOM-UR-00003204-05.

and fees from insulin manufacturers. To be clear, PBMs have an incentive for manufacturers to keep list prices high, since the rebates, discounts, and fees PBMs negotiate are based on a percentage of a drug's list price—and PBMs retain at least a portion of what they negotiate. In fact, the investigation found instances in which insulin manufacturers were dissuaded from setting lower list prices for their products, which would have likely lowered out-of-pocket costs for patients, due to concerns that PBMs and health plans would react negatively.

Lastly, it is clear that the average net prices for insulin—that is, the revenue manufacturers receive after paying rebates—have declined in recent years due to the growth of rebate sizes. However, manufacturers are still retaining higher average net prices, and thus, generating more revenue per unit of insulin, than they were during the first decade of the 21st century. Large rebates have shrunk the percentage of gross revenue that manufacturers retain, but the exponential growth of WAC prices over the last 20 years has benefited insulin manufacturers by slowing margin declines, and PBMs by increasing revenue derived from rebates and fees.

In recent years, Senator Grassley and Senator Wyden have worked together to bring unparalleled transparency to pharmaceutical pricing and marketing. While this investigation was focused on insulin, it brings Congress and the public one step closer to better understanding the complex market dynamics of the U.S. drug pricing system. Undoubtedly, there is more work to be done. The Committee will continue to shed light on pharmaceutical pricing practices that cause financial harm and worse health outcomes for the American people.

Appendix

Documents Produced by

OptumRx

Response to 1a and 1c

OptumRx administers pharmacy benefits for its health plan customers, on whose behalf the Company negotiates prescription drug discounts. In that context, OptumRx contracts with the following insulin manufacturers: Sanofi-Aventis, U.S., LLC ("Sanofi"), Eli Lilly and Company ("Eli Lilly"), and Novo Nordisk, Inc. ("Novo Nordisk").

Drug manufacturers independently set the prices for the products they manufacture and market. OptumRx cannot and does not set these list prices. OptumRx does work to reduce the net price its customers pay for drugs through vigorous discount negotiations with manufacturers. OptumRx has negotiated discounts with Sanofi, Eli Lilly, and Novo Nordisk for insulin products and certain other prescription drugs that the companies manufacture.

Additionally, to discourage list price increases and keep net costs as low as possible for its customers, OptumRx negotiates price protection guarantees with drug manufacturers. These guarantees trigger additional discounts if the manufacturer increases the price of a drug above a negotiated threshold. OptumRx has negotiated price protection guarantees with each of the insulin manufacturers with whom it contracts.

OptumRx passes on approximately 98 percent of its negotiated discounts to its customers, which in turn decide how to pass that value onto individual consumers—either through direct point-of-sale discounts, lower premiums, or both. In those limited instances in which OptumRx retains a portion of a discount, it is because the Company's customers have chosen to compensate it that way. OptumRx passes on an even greater percentage of negotiated discounts to government plan customers.

OptumRx performs various services in connection with the administration of its negotiated discounts, in exchange for which it receives administrative fees from insulin manufacturers. OptumRx also passes on the value of these administrative fees to its customers in many circumstances, pursuant to the terms of its customer agreements. OptumRx does not perform consultative services for insulin manufacturers.

Response to 4a, 4b and 4d

OptumRx's formulary design and management is focused on providing access to high-quality, clinically appropriate, cost-effective products. As a general matter, the design of plan formularies follows a multi-step process.

First, OptumRx's Pharmacy & Therapeutics ("P&T") Committee, described in greater detail below, evaluates clinical evidence to assess a medication's role in therapy and overall clinical value. The P&T Committee provides evidence-based review and appraisal of new drugs, existing drugs, and their appropriate places in therapy. As necessary, the P&T Committee will review and evaluate medical criteria, standards, and educational intervention methods in the process of developing clinical recommendations for drugs and drug management.

Second, subject to the clinical designations and recommendations of the P&T Committee, OptumRx makes decisions regarding the placement of prescription drugs on OptumRx's standard formularies. Its primary goal in doing so is to design standard formularies that are attractive to current and potential customers, particularly by providing customers with the lowest possible net cost of drugs.

Additionally, formulary and utilization management decisions are ultimately the authority of OptumRx's customers, which retain complete and exclusive control over their own benefit plans—including formulary design. OptumRx designs standard national formularies based upon objective evaluation of the therapeutic merits, safety, and cost of available prescription drugs. OptumRx's customers may select one or more of these standard formularies as the basis for their pharmacy benefit plan, or may opt to establish their own tailored formularies. OptumRx may also assist customers with the administration of their custom formularies.

OptumRx's P&T Committee is an independent advisory body that evaluates existing and emerging drugs based on scientific evidence. It reviews and appraises those drugs in an evidenced-based manner. Membership on the P&T Committee currently consists of 11 members from a range of specialties, including ten physicians and a pharmacist. To ensure that P&T Committee recommendations are independent and unbiased, no Committee member is an employee or client of OptumRx, or a drug manufacturer representative, and each member must sign conflict of interest disclosures.

The P&T Committee meets several times per year, sometimes in person and sometimes by teleconference, to make, review, update, develop and approve clinical recommendations regarding placement of new drugs on OptumRx standard formularies, procedures for formulary management activities such as prior authorizations and step-therapies, drug utilization management strategies, and clinical educational programs.

The P&T Committee commences a drug review upon the release of a new drug, including a new FDA-approved indication for an existing drug, a new FDA-approved formulation for an existing chemical entity, or release of a new strength of an existing product. Where a new drug is part of an existing therapeutic drug class, a new drug review will often require review of other drugs within that class. The P&T Committee's reviews are based on scientific evidence and standards of practice; drug discounts are not considered during P&T Committee reviews and do not factor into the Committee's evaluation.

Each P&T Committee review results in one or more clinical drug recommendations to OptumRx. Recommendations can include, for example, designation of a drug or drug class as: "Essential Drug," "Essential Class," "Unique Risk," "Additional Data Required," "Optional Inclusion," "Non-Essential Non-FDA-Approved Drug," or "Vaccine."

Subject to the clinical designations and recommendations of the P&T Committee, OptumRx makes decisions regarding formulary placement of FDA-approved prescription drugs for its standard formularies. OptumRx recommendations regarding formulary placement are also shared with certain OptumRx clients that choose to create and follow custom formularies. Such OptumRx customers are the final decision-makers for any custom client-specific formularies.

OptumRx's primary goal is to promote the highest quality, cost-effective products and achieve the lowest possible net cost of drugs for OptumRx's customers, including the promotion of lower-cost generic drugs where they are available.

OPTUMRx

OptumRx Pharmacy and Therapeutics (P&T) Committee Quarterly Meeting Agenda Summary

August 2016

New Drug Reviews	Therapeutic Class Reviews	Re-classifications
• **Basaglar** (LY insulin glargine U- [redacted]	[redacted]	[redacted] **Lantus Solostar** (insulin glargine U-100) injection; **Levemir, Levemir FlexTouch** (insulin detemir U-100) injection; **Toujeo SoloStar** (insulin glargine U-300) injection [redacted]

Note: Brand names are indicated by bolded text; generic-only products are indicated by non-bolded text

NEW DRUG REVIEW – Basaglar
RECLASSIFICATION – Long-acting Insulin Agents

Medication	Previous P&T Recommendation	Previous Clinical Notes	Current P&T Recommendation	Current Clinical Notes	UM†
Basaglar (LY insulin glargine U-100) injection	N/A	N/A	**Essential Class** (long acting insulin analogs; long acting insulin analogs are the preferred basal insulin therapy due to lower hypoglycemic rates compared to intermediate-acting insulin NPH; in clinical trials and using indirect comparisons, long-acting insulin agents are similarly effective in achieving and maintaining glycemic control and have mostly similar rates	• Pharmacokinetic and pharmacodynamic (PK/PD) differences may result in: ○ A steadier PK/PD profile for Toujeo with a potentially smoother insulin effect ○ Potential for twice-daily dosing with Levemir	ST
Lantus, Lantus Solostar (insulin glargine U-100) injection	**Essential Class** (long acting insulin analogs; long acting insulin analogs are the preferred basal insulin therapy due to lower hypoglycemic rates compared to intermediate-acting insulin NPH) (5/2015)	• In clinical trials, Lantus and Levemir are similarly effective in achieving and maintaining glycemic control and they have similar rates of hypoglycemia; however, due to pharmacokinetic and pharmacodynamic differences, higher doses of total basal			--
Levemir, Levemir FlexTouch (insulin detemir U-100) injection					--
Toujeo SoloStar (insulin glargine U-300) injection					--

		insulin and twice-daily dosing are often required with Levemir compared to Lantus.	of hypoglycemia)		
Therapeutic Class: Antidiabetic agents, Insulin					

†An asterisk next to the UM type indicates UM programs that were reviewed and approved at the August 2016 P&T meeting; all others indicate existing UM

Indications

- Basaglar (LY insulin glargine) is indicated to improve glycemic control in adults and pediatric patients with type 1 diabetes mellitus (T1DM) and in adults with type 2 diabetes mellitus (T2DM).
- Limitations of use: Not recommended for the treatment of diabetic ketoacidosis.

Summary

Background

- Long-acting insulin analogs (Levemir [insulin detemir], Tresiba [insulin degludec], Lantus and Toujeo [insulin glargine]) are the mainstay of basal insulin therapy in patients with diabetes mellitus. In December 2015, long-acting insulin, Basaglar (LY insulin glargine), was Food and Drug Administration (FDA)-approved by standard review.
  - Based on pharmacokinetic data, Toujeo and Tresiba have a longer duration of action (greater than 24 hours) compared to the other long-acting insulin agents, which allows greater flexibility in administration times.
  - Levemir is the only long-acting insulin with a peak seen anywhere from 4 to 12 hours post-dose (*Prescribing information: Basaglar, 2016; Lantus, 2015; Levemir, 2015; Toujeo, 2015; Tresiba, 2015*).
- The New Drug Application (NDA) for Basaglar evaluated by standard review was tentatively approved by the FDA in 2014.
  - The final FDA-approval of Basaglar could not commence until the end of an automatic stay of 30 months due to patent infringement litigation filed by Sanofi. The final FDA-approval of Basaglar was granted on December 16, 2015. Under the settlement agreement, the United States (US) launch of Basaglar may occur on December 15, 2016 (*Drugs@FDA 2016; Eli Lilly press release 2015; FDA approval letter 2014*).
  - In October 2014, LY insulin glargine (Abasaglar) was the first biosimilar insulin approved for marketing authorization in Europe (*European Medicines Agency [EMA] summary, 2014*). LY insulin glargine is not considered a biosimilar in the US, but is considered a "follow-on biologic" to Lantus. A handful of biologics are evaluated by the FDA under the 505(b)(2) pathway under the Federal Food, Drug, and Cosmetic Act (FD&C Act). In March of 2016, the FDA released draft guidance interpreting the Biologics Price Competition and Innovation Act (BPCIA) to mean that all biologics approved under the 505(b)(2) path will be considered approved under the 351 path, known as the "biosimilar pathway," after March 23, 2020 (*FDA guidance for industry 2000; FDA guidance for industry 2016; FDA press release, 2016; Howard et al 2015; Shehan et al 2016*).

Clinical trial data

- The safety and efficacy of LY insulin glargine compared to insulin glargine were evaluated through 2 pivotal studies in approximately 1300 patients with T1DM through the ELEMENT 1 trial, or T2DM through the ELEMENT 2 trial. Both trials were multicenter (MC), parallel group (PG), randomized controlled trials (RCTs); ELEMENT 1 was open-label (OL) and ELEMENT 2 was double-blinded (DB). Both trials were conducted over 24 weeks; however, ELEMENT 1 also included a 28-week comparative safety extension period. The primary efficacy endpoint tested the non-inferiority of agents by the reduction in (hemoglobin A1c [HbA1c]) from baseline to 24 weeks, and key secondary endpoints included overall and severe hypoglycemic events and mean weight change (*Basaglar prescribing information 2016*; *Blevin et al 2015; Rosenstock et al 2015*).
  - Based on the primary analysis, a non-inferiority margin of 0.4% was tested. If this was met, a non-inferiority margin of 0.3% was also tested.
  - Dose adjustments were only made after week 12 in the case of safety concerns.
  - Mealtime insulin lispro was administered 3 times daily in both groups within the ELEMENT 1 trial. Oral antidiabetic medication was permitted in conjunction with insulin treatment within the ELEMENT 2 trial.

Table 1. Summary of results from the ELEMENT trials

Patient Group	T1DM		T2DM
Study name (Weeks)	ELEMENT 1 (24)	ELEMENT 1 (52)	ELEMENT 2 (24)

Comparators* (n)	LY IGlar (n = 268*)	IGlar (n = 267)	LY IGlar (n = 268*)	IGlar (n = 267)	LY IGlar (n = 376*)	IGlar (n = 380)
HbA1c						
Baseline, mean ± SD	7.75 ± 1.13	7.79 ± 1.03	7.75 ± 1.13	7.79 ± 1.03	8.34 ± 1.09	8.31 ± 1.06
Change from baseline, %†‡	-0.35	-0.46	-0.26	-0.28	-1.29	-1.34
LSMD†‡ (95% CI)	0.108 (-0.002 to 0.219)		0.020 (-0.099 to 0.140)		0.052 (-0.070 to 0.175)	
Hypoglycemia‖, events/patient/year ± SD						
Overall ± SD	86.5 ± 77.3	89.2 ± 80.1	77.0 ± 68.7	79.8 ± 74.5	21.3 ± 24.4	22.3 ± 28.2
Severe ± SD	0.06 ± 0.52	0.09 ± 0.50	0.07 ± 0.46	0.08 ± 0.46	0.04 ± 0.66	0.01 ± 0.16
Weight gain						
LS mean increase in weight, kg	0.36	0.12	0.71	0.36	1.8	2.0

Abbreviations: CI = confidence interval; HbA1c = hemoglobin A1c; IGlar = insulin glargine (Lantus); LS = least square; LSMD = least square mean difference; LY IGlar = insulin glargine (Basaglar); SD = standard deviation

*One patient randomized in the ELEMENT 1 trial and 3 patients randomized in the ELEMENT 2 trial in the LY IGlar group was not included in the full analysis set (FAS).

†ANCOVA model includes treatment, country, sulfonylurea use (for the ELEMENT 2 trial only), and time of baseline basal insulin injection (daytime or evening/bedtime) as fixed effects and baseline HbA1c as covariate.

‡The results were calculated based on the number of patients in the FAS using their last observed post-baseline value of HbA1c. Observed HbA1c data at 24 weeks were available from 256 (95.5%) and 258 (96.6%) subjects randomized to the ELEMENT 1 LY IGlar and comparator IGlar groups, respectively; and 331 (88%) and 329 (87%) subjects randomized to the ELEMENT 2 LY IGlar and comparator IGlar groups, respectively.

‖The overall rate at 24 or 52 weeks accounts for all events reported during the 24- or 52-week treatment period.

  - LY insulin glargine was non-inferior to insulin glargine for the reduction in HbA1c. No statistically significant differences were observed between endpoints outlined in Table 1.

Safety

- LY insulin glargine has similar contraindications and warnings and precautions as other insulin glargine products.
- The most common adverse events (incidence ≥ 5%) with LY insulin glargine use are hypoglycemia, allergic reactions, injection site reaction, lipodystrophy, pruritus, rash, edema, and weight gain. Additional adverse reactions include infection, nasopharyngitis, and upper respiratory tract infection. As with all therapeutic proteins, there is potential for immunogenicity. In T1DM patients, a total of 65% had detectable antibodies to insulin at 52 weeks and in T2DM patients, 51% had detectable antibodies to insulin at 24 weeks. There is no evidence that the antibodies had any impact on efficacy and safety outcomes (*Basaglar prescribing information 2016*).

Guidelines

- According to the American Diabetes Association (ADA) treatment guidelines for diabetes, most individuals with T1DM should be treated with multiple-dose insulin or continuous subcutaneous insulin infusion. In contrast, the ADA and the American Association of Clinical Endocrinologists (AACE) recommend a patient-centered approach to guide the choice of pharmacological agents for the treatment of T2DM. Considerations include efficacy, cost, potential side effects, comorbidities, hypoglycemia risk, and patient preferences (*Garber et al 2016; Handelsman et al 2015; ADA 2016*).
  - Treatment guidelines from the ADA and AACE have not been updated to include LY insulin glargine; however, it is anticipated that treatment will follow that of insulin glargine.

Dosing

- Patients may administer 1 to 80 units of LY insulin glargine subcutaneously per injection once daily at any time during the day but at the same time every day. Patients may inject. Individualized dosing is recommended based on metabolic needs, blood glucose monitoring, glycemic control, type of diabetes, and prior insulin use of the patient (*Basaglar prescribing information 2016*).

Conclusion

- Basaglar (LY insulin glargine) is a follow-on biologic to similar to Lantus (insulin glargine). Based on 2 non-inferiority trials, LY insulin glargine and insulin glargine appear to be similarly effective in achieving and maintaining glycemic control in T1DM and T2DM patients. ELEMENT 1 and 2 did not reveal any significant differences in the incidence of antibodies, body weight changes, the rate of hypoglycemia, and the incidences of adverse events (overall, serious,

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Response to 3

Drug manufacturers, including insulin manufacturers, independently set the prices for the products they manufacture and market. OptumRx does not set or affect these list prices. Instead, OptumRx works to reduce the net price its customers pay for drugs through vigorous discount negotiations with manufacturers. OptumRx's Industry Relations group negotiates contracts and discounts with drug manufacturers, including manufacturers of insulin. Industry Relations plays no role in the independent clinical evaluation by, or resulting recommendations from, OptumRx's Pharmacy and Therapeutics Committee.

OptumRx utilizes purchasing volume and other market forces to negotiate discounts with manufacturers and offer price predictability to its customers. The manner in which OptumRx negotiates these discounts varies case-to-case, but in general the discounts are predicated on an analysis of marketplace trends and predictions about what the market for insulin pricing will be when the contract at issue takes effect. OptumRx has negotiated discounts and price protection guarantees with each insulin manufacturer with whom it currently contracts.

OptumRx regularly communicates with manufacturers regarding discounts. For example, following the release of a new drug into the market, a revised P&T Committee classification, or a regular therapeutic class review, Industry Relations may initiate discussions with a manufacturer regarding the potential for improved discount terms. In other cases, a manufacturer may initiate contact with OptumRx to propose new or different discount structures.

OptumRx's customers may choose to manage insulin utilization through the use of evidence-based utilization management tools (for instance, step edits or exclusions), or they may have an open benefit design where all products are available at a similar co-payment for members. Price concessions offered by manufacturers may depend on the level of control that OptumRx's customers exercise over insulin utilization, with higher control yielding higher discounts and thus lower net costs. But the discount structures OptumRx negotiates with insulin manufacturers permit OptumRx's customers to place a full range of insulin products on Tier 1 of their formularies—the tier usually reserved for generics, and that usually results in the lowest co-payment for members. A majority of OptumRx's customers place insulin products on that tier.

Response to 1.d:

OptumRx currently contracts with the following insulin manufacturers: Sanofi-Aventis, U.S., LLC ("Sanofi"), Eli Lilly and Company ("Eli Lilly"), and Novo Nordisk, Inc. ("Novo Nordisk"). OptumRx's agreements with the manufacturers have not been terminated before their expiration dates.

Response to 4.b:

The members of the OptumRx Pharmacy and Therapeutics Committee ("P&T Committee") for the period from 2016 to the present are listed below:

P&T Committee Member	Degree
Alexander, Caleb	M.D.
Chan, Paul	M.D.
Gandhi, Darshan	M.D.
Karlamangla, Arun	M.D.
Koronowski, Michael	Pharm.D.
Kowaloff, Ed	M.D.
Lewis, Stuart	M.D.
McQuaid, Ken	M.D.
Polston, Gregory	M.D.
Potter, Jeffrey	M.D.
Shuster, John	M.D.
Stein, Regina	M.D.
Swarr, Peter	M.D.

OPTUMRx®

Therapeutic Class Review
Rapid-Acting Insulins

MEDICATION*	MARKETER	AVAILABILITY
Admelog (insulin lispro) injection	Sanofi-Aventis	**Brand:** 100 units/mL (U100) in 10 mL multiple-dose vial and 3 mL SoloStar prefilled pen
Afrezza (insulin human) inhalation powder	Mannkind Corp.	**Brand:** 4, 8, 12 unit single-use cartridges
Apidra (insulin glulisine) injection	Sanofi-Aventis	**Brand:** U100 in 10 mL multiple-dose vial and 3 mL SoloStar prefilled pen
Fiasp (insulin aspart) injection	Novo Nordisk	**Brand:** U100 in 10 mL multiple-dose vial and 3 mL FlexTouch prefilled pen
Humalog (insulin lispro) injection	Eli Lilly	**Brand:** U100 in 3 mL, 10 mL multiple-dose vials, 3 mL KwikPen and Junior KwikPen prefilled pens, 3 mL cartridges; U200 in 3 mL KwikPen prefilled pens
Novolog (insulin aspart) injection	Novo Nordisk	**Brand:** U100 in 10 mL multiple-dose vial, 3 mL PenFill cartridges, 3 mL FlexPen prefilled pens
Purpose of Review: To evaluate the safety and efficacy of the rapid-acting insulins, including Admelog, a new follow-on insulin lispro formulation, for formulary consideration.		

*Brand names are indicated by bolded text; generic-only products are indicated by non-bolded text

Note: Information on indications, pharmacology, dosing, and safety has been obtained from the prescribing information for the individual products, except where noted otherwise.

SUMMARY

Background

- In 2015, an estimated 30.3 million people, or 9.4% of the United States (US) population, had diabetes mellitus (DM); as many as 7.2 million were undiagnosed *(Centers for Disease Control and Prevention [CDC] 2017)*.
- Individuals with type 1 diabetes mellitus (T1DM) account for 5% of the overall DM population; T1DM is a result of autoimmune pancreatic β-cell destruction that leads to absolute insulin deficiency. Type 2 diabetes mellitus (T2DM) accounts for 90 to 95% of the DM population and is characterized by both insulin resistance and relative insulin deficiency; risk factors for the development of T2DM include aging, obesity, and physical inactivity *(American Diabetes Association [ADA] 2017, McCulloch 2016)*.
  - T1DM is treated with multiple daily injections of prandial and basal insulin or continuous subcutaneous insulin infusion (CSII) with a rapid-acting insulin analog.
  - Pharmacologic options for T2DM include first-line metformin and second- or third-line oral antidiabetic drugs (OADs) such as sulfonylureas (SFUs), thiazolidinediones (TZDs), meglitinides (GLNs), dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors and the injectable agents, glucagon-like peptide-1 (GLP-1) receptor agonists and insulin products .
- Rapid-acting insulin analogs have more rapid absorption, faster onset of action, and shorter duration of action than regular insulin due to modifications of the insulin molecule that prevent it from forming hexamers or polymers that slow absorption and delay action. These rapid-acting insulin analogs better mimic endogenous insulin production and allow more flexibility in administration around meals than regular insulin *(McCulloch 2016)*.

Available Products

- There are currently 6 rapid-acting insulins approved by the Food and Drug Administration (FDA) *(FDA Web site)*.
  - The first rapid-acting insulin analogs, Humalog (insulin lispro) and Novolog (insulin aspart) received FDA approval in 1996 and 2000, respectively. Apidra (insulin glulisine) was approved in 2004.
  - Afrezza (insulin human), FDA approved in 2014, is the only available inhaled insulin.
  - Fiasp (insulin aspart) was FDA approved in September 2017 and is comprised of insulin aspart with the addition of niacinamide; nonclinical data have demonstrated that the addition of niacinamide promotes the formation of insulin aspart monomers after subcutaneous (SC) injection, facilitating a more rapid rate of insulin aspart absorption across

the endothelium into the blood *(Russell-Jones et al 2017)*.
  - Admelog (insulin lispro) was FDA approved in December 2017 via the 505(b)(2) pathway and is the first follow-on rapid-acting insulin.
- Admelog, Apidra, Humalog, and Novolog are indicated to improve glycemic control in adults and children with DM. Fiasp and Afrezza are indicated to improve glycemic control in adults with DM.
  - Afrezza must be used with a long-acting insulin in patients with T1DM and is not recommended in patients who smoke or for treating diabetic ketoacidosis.

Clinical Efficacy
- The safety and efficacy of Humalog and Novolog have been well-established in the various DM populations *(Fullerton et al 2016, Plank et al 2005)*.
  - In a systematic review (SR) and meta-analysis (MA) evaluating randomized controlled trials (RCTs) (42 trials; N = 7933 patients) of Humalog or Novolog vs regular insulin, glycosylated hemoglobin (HbA1c) reduction was comparable across T1DM, T2DM, and gestational diabetes patients. In T1DM, a minor, statistically significant benefit was identified in HbA1c lowering (weighted mean difference: -0.12%; 95% confidence interval [CI], -0.17 to -0.07%). No significant differences were identified in rates of hypoglycemia *(Plank et al 2005)*
  - In a Cochrane Review evaluating RCTs (9 trials; N = 2693 patients) of Humalog and Novolog vs regular insulin in T1DM, the mean difference in HbA1c was -0.15% (95% CI, -0.2 to -0.1%; p < 0.00001; low quality evidence) in favor of rapid-acting insulins. There were no substantial differences in rates of overall hypoglycemia between the groups. The comparison of the risk of severe hypoglycemia between the 2 treatments showed an odds ratio (OR) of 0.89 (95% CI, 0.71 to 1.12; p = 0.31; 7 trials, very low quality evidence) *(Fullerton et al 2016)*.
- The safety and efficacy of Apidra were evaluated in several 26-week, open-label (OL), parallel-group (PG) RCTs vs regular insulin or Humalog. In a trial enrolling T2DM patients (N = 876) on insulin therapy *(Dailey et al 2004)*, a slightly greater HbA1c reduction from baseline to 26 weeks was seen with Apidra vs regular insulin (-0.46% vs -0.30%; p = 0.0029). In a similar trial *(Rayman et al 2007)* in the same patient population (N = 890), no differences in baseline to endpoint HbA1c reductions were seen (Apidra -0.32%; regular insulin -0.35%; p = 0.5726), but Apidra statistically significantly lowered post-prandial glucose (PPG) more at 2 hours. When Apidra was compared to Humalog in a basal/bolus regimen in T1DM patients (N = 683), no significant differences in HbA1c lowering or rates of hypoglycemia were identified *(Dreyer et al 2005)*.
- Afrezza was evaluated in both T1DM and T2DM patients. In a 24-week OL, active-comparator (AC), noninferiority trial, patients with T1DM on basal insulin were randomized to receive prandial Afrezza or Novolog. Afrezza met the prespecified noninferiority margin of 0.4% reduction of HbA1c from baseline, but reductions were significantly less with Afrezza compared to Novolog and fewer Afrezza patients achieved an HbA1c target of < 7% *(Bode et al 2015)*. T2DM patients inadequately controlled on OADs were randomized to receive Afrezza or placebo in a double-blind (DB) trial. At week 24, treatment with Afrezza provided a statistically significantly greater mean reduction in HbA1c than placebo *(Rosenstock et al 2015[a])*.
- Fiasp was evaluated in the Onset clinical trial program. Onset 1 *(Russell-Jones et al 2017)* was a 26-week, Phase 3, AC, RCT that compared Fiasp (mealtime and postmeal) to Novolog in patients with T1DM. Both mealtime and postmeal Fiasp were demonstrated to be noninferior to Novolog in change in HbA1c (estimated treatment difference [ETD], -0.15; p < 0.0001; ETD 0.04%; p < 0.0001, respectively). Onset 2 *(Bowering et al 2017)* was a 26-week, Phase 3, DB, AC, RCT in T2DM patients on insulin and OADs. Patients were randomized to receive mealtime Fiasp (n = 345) or Novolog (n = 344). Fiasp demonstrated noninferiority to Novolog in HbA1c lowering (ETD -0.02%; p < 0.0001). Onset 3 *(Rodbard et al 2017)* was an 18-week, Phase 3, OL, RCT in T2DM patients inadequately controlled on basal insulin and OADs. Patients were randomized to receive mealtime Fiasp + basal insulin (n = 116), or basal insulin alone (n = 120). The addition of Fiasp to basal insulin demonstrated superior HbA1c lowering from baseline (ETD -0.94%; p < 0.0001 for superiority) and significantly more patients achieved an HbA1c < 7.0% (60.3% vs 18.3%; OR, 9.31; p < 0.0001); however, with the addition of Fiasp, there was an increase in the frequency of severe or blood glucose (BG)-confirmed hypoglycemic episodes (rate ratio [RR], 8.24; p < 0.0001) and modest weight gain.
- The safety and efficacy of Admelog were evaluated in two 26-week, Phase 3, OL, PG, RCTs in both T1DM (N = 506) (SORELLA 1; *Garg et al 2017)* and T2DM (N = 505) patients (SORELLA 2; *Derwahl et al 2018)*. Patients were randomized to receive Admelog or its reference product, Humalog. Change in HbA1c in Admelog-treated patients was found to be noninferior in both trials (SORELLA 1: least squares [LS] mean difference, 0.06%; 95% CI, -0.084 to 0.197; SORELLA 2: LS mean difference, -0.07%; 95% CI, -0.215 to 0.067). Rates of hypoglycemia were similar between the treatment arms in both trials.

Place in Therapy
- Rapid-acting insulin analogs are an important part of T1DM insulin therapy and are often utilized in T2DM when escalation of therapy is required. Guidelines from the ADA and the American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE) recommend basal insulin plus prandial insulin, or CSII with rapid-acting insulin for patients with T1DM; rapid-acting insulin analogs are preferred over regular insulin in

T1DM as they carry less hypoglycemia risk. Patients with T2DM unable to maintain glycemic control on OADs should be considered for basal insulin therapy and subsequently intensified to combination injectable therapy with a GLP-1 receptor agonist or prandial insulin if additional glycemic control is needed. No injectable rapid-acting insulin analog is preferred over another; the guidelines have not been updated to address Admelog *(ADA 2018, Garber et al 2018)*.

Safety

- The rapid-acting insulins are contraindicated during episodes of hypoglycemia and have warnings for hypoglycemia, hypokalemia, hypersensitivity reactions, and fluid retention and heart failure with concomitant use of TZDs.
  - Afrezza is additionally contraindicated in chronic lung disease, such as asthma or chronic obstructive pulmonary disease (COPD). Afrezza has a boxed warning for bronchospasm in patients with chronic lung disease. Additionally, Afrezza has a warning for lung cancer and should not be used in patients with active lung cancer. In patients with a history of lung cancer or at risk for lung cancer, the benefit of Afrezza use should outweigh this potential risk.
- The most common adverse effects (AEs) associated with the injectable rapid-acting insulins include hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, and rash. Common AEs for Afrezza include hypoglycemia, cough, and throat pain or irritation.

Dosing

- The dosage of rapid-acting insulins should be individualized based on the patient's metabolic needs, BG monitoring results, and glycemic control goal. Rapid-acting injectable insulins should be administered SC just prior to or immediately following a meal. Afrezza should be inhaled at each meal as directed. Additionally, Admelog, Apidra, Humalog (U100), and Novolog are indicated for use as CSII; product- and pump-specific instructions should be followed.
- The pharmacologic profiles of the rapid-acting insulin analogs are comparable (see Table 1).

Table 1. Pharmacologic characteristics of rapid-acting insulins *(Facts and Comparisons Web site 2018)*

Insulin	Onset (hrs)	Peak Glycemic Effect (hrs)	Duration (hrs)
Admelog (insulin lispro)	0.25 to 0.5	0.5 to 2.5	≤ 5
Afrezza (insulin human)	~0.25	~0.88	2.5 to 3
Apidra (insulin glulisine)	0.2 to 0.5	1.6 to 2.8	3 to 4
Fiasp (insulin aspart)	~0.2 to 0.3	~1.5 to 2.2	~5 to 7
Humalog (insulin lispro)	0.25 to 0.5	0.5 to 2.5	≤ 5
Novolog (insulin aspart)	0.2 to 0.3	1 to 3	3 to 5

Conclusion

- The rapid-acting insulins have established efficacy and safety in both the T1DM and T2DM populations. The injectable agents are guideline-recommended for T1DM due to less hypoglycemia risk vs regular insulin.
- The injectable rapid-acting insulins have demonstrated comparable HbA1c lowering in clinical trials. Newly-approved Admelog, the first follow-on rapid-acting insulin, demonstrated noninferiority to its reference drug Humalog in RCTs in both T1DM and T2DM patients. Afrezza, the only inhalation rapid-acting insulin, demonstrated noninferior HbA1c lowering vs Novolog, but reductions were significantly less with Afrezza and fewer Afrezza patients achieved an HbA1c target of < 7%.
- Safety profiles of the injectable rapid-acting insulins are comparable. Afrezza has a boxed warning for bronchospasm and is contraindicated in patients with chronic lung disease.

BACKGROUND

- In 2015, an estimated 30.3 million people, or 9.4% of the US population, had DM; as many as 7.2 million were undiagnosed *(CDC 2017)*.
- Individuals with T1DM account for 5% of the overall DM population. Insulin is the mainstay of therapy in these patients, as autoimmune pancreatic β-cell destruction typically leads to absolute insulin deficiency. Most patients with T1DM require treatment with multiple daily injections of prandial insulin and basal insulin or CSII. The use of rapid-acting insulin analogs in these patients reduces hypoglycemia risk vs regular insulin *(ADA 2017)*.
- T2DM accounts for 90 to 95% of the DM population and is characterized by both insulin resistance and relative insulin deficiency. Patients are typically started on non-pharmacologic interventions (eg, diet, exercise, weight loss) and OADs, such as metformin. Addition of insulin is indicated if goal glycemic control is not attained. Initiation of insulin therapy is often delayed due to clinician or patient reluctance; however, most patients with T2DM will eventually require insulin therapy due to the decline in endogenous insulin production. Basal insulin is typically initiated and optimized before prandial dosing with rapid-acting or regular insulin is considered *(McCulloch 2016)*.
  - Both basal and prandial insulin regimens have demonstrated similar efficacy in reduction of HbA1c concentrations when titrated to achieve glycemic goals in T2DM; however, basal insulin is associated with less frequent hypoglycemia and greater patient satisfaction *(McCulloch 2017)*.

- Rapid-acting insulin analogs have more rapid absorption, faster onset of action, and shorter duration of action than regular insulin due to modifications of the insulin molecule that prevent it from forming hexamers or polymers that slow absorption and delay action. These rapid-acting insulin analogs better mimic endogenous insulin production and allow more flexibility in administration around meals than regular insulin *(McCulloch 2016)*.
- The pharmacologic profiles of the injectable rapid-acting insulin analogs are comparable (see Table 3).
- The first rapid-acting insulin analogs, Humalog (insulin lispro) and Novolog (insulin aspart) received FDA approval in 1996 and 2000, respectively. Apidra (insulin glulisine) was approved in 2004 *(FDA Web site)*.
- Fiasp (insulin aspart) was FDA approved in September 2017 and consists of insulin aspart with the addition of niacinamide; nonclinical data have demonstrated that the addition of niacinamide promotes the formation of insulin aspart monomers after SC injection, facilitating a more rapid rate of insulin aspart absorption across the endothelium into the blood *(FDA Web site, Russell-Jones et al 2017)*.
- Admelog (insulin lispro) was FDA approved in December 2017 via the 505(b)(2) pathway and is the first follow-on rapid-acting insulin *(FDA Web site)*.
- Afrezza (insulin human), FDA approved in 2014, is the only available inhaled insulin and is approved for prandial dosing; noninferiority in HbA1c lowering was demonstrated in a head-to-head trial with Novolog, although the mean HbA1c reduction was greater with Novolog and more patients in the Novolog arm achieved HbA1c goals of ≤ 7% and ≤ 6.5% *(Bode et al 2015)*. Afrezza is contraindicated in patients with chronic lung disease such as asthma or COPD and has a boxed warning for bronchospasm in this patient population.

INDICATIONS

Table 2. FDA-approved indications for the rapid-acting insulins

Drug	Improve glycemic control in adults and children with diabetes mellitus	Improve glycemic control in adults with diabetes mellitus
Admelog (insulin lispro)	✓	
Afrezza (insulin human)		✓*
Apidra (insulin glulisine)	✓	
Fiasp (insulin aspart)		✓
Humalog (insulin lispro)	✓	
Novolog (insulin aspart)	✓	

*Limitations of use: Must use with a long-acting insulin in patients with T1DM. Not recommended for treating diabetic ketoacidosis. Not recommended in patients who smoke.

PHARMACOLOGY

Table 3. Pharmacologic characteristics of rapid-acting insulins *(Facts and Comparisons Web site 2018)*

Insulin	Onset (hrs)	Peak Glycemic Effect (hrs)	Duration (hrs)
Admelog (insulin lispro)	0.25 to 0.5	0.5 to 2.5	≤ 5
Afrezza (insulin human)	~0.25	~0.88	2.5 to 3
Apidra (insulin glulisine)	0.2 to 0.5	1.6 to 2.8	3 to 4
Fiasp (insulin aspart)	~0.2 to 0.3	~1.5 to 2.2	~5 to 7
Humalog (insulin lispro)	0.25 to 0.5	0.5 to 2.5	≤ 5
Novolog (insulin aspart)	0.2 to 0.3	1 to 3	3 to 5

CLINICAL EFFICACY

STUDY DESIGN ABBREVIATIONS: AC = active control; CI = confidence interval, DB = double-blind; HR = hazard ratio; MC = multi-center; OL = open-label; OR = odds ratio; PC = placebo-controlled; PG = parallel-group; RCT = randomized controlled trial; RR = relative risk; SB = single-blind; SC = single-center; XO = crossover

***Search Strategy**: Studies supporting the FDA-approved indications were identified using search terms "insulin aspart, insulin lispro, insulin glulisine, rapid-acting insulins" and "diabetes" February 7, 2018. Manufacturer submitted data were also reviewed when available. A comprehensive PubMed literature search was performed for human studies published in English. Assessment of each study's design (eg, randomization, blinding methodology, appropriateness of treatment outcomes, etc.), validity and importance was completed. Review of patient data in groups to which they were randomized (intention to treat analysis), accounting for patient withdrawals, and baseline characteristics was completed.*

<u>Admelog (insulin lispro)</u>

Study 1. Garg et al, *Diabetes Technol Ther.* 2017;19(9):516-526. SORELLA 1

Study Objective: Evaluate the safety, efficacy, and immunogenicity of Admelog vs Humalog in adult patients with

T1DM	
Study Design, Follow-up	**Treatment Groups**
• 26-week, Phase 3, MC, OL, PG, RCT ○ The main study period was followed by a 26-week safety extension.	• Admelog SC before meals with basal insulin glargine U100 (n = 253) • Humalog SC before meals with basal insulin glargine U100 (n = 254) • The starting doses of Admelog and Humalog were based on a unit-to-unit conversion from the patients' previous rapid-acting insulin dose. • Admelog and Humalog doses were titrated based on a 2-hr PPG goal of 120 to 160 mg/dL. Patients were instructed to self-adjust doses according to local guidelines. • Insulin glargine U100 was maintained at the pre-study dose and given once daily at the same time as used before study initiation. • The basal insulin fasting prebreakfast goal was between 80 to 130 mg/dL. There was no formal titration algorithm for basal insulin.
Inclusion Criteria	**Exclusion Criteria**
• ≥ 18 years of age with T1DM diagnosed for at least 12 months • HbA1c ≥ 7 and ≤ 10% • Treated with insulin glargine as basal insulin and Humalog or Novolog as rapid-acting mealtime insulin for at least 6 months	• Body mass index (BMI) ≥ 35 kg/m^2 • Use of noninsulin antidiabetic treatments or the use of CSII • History of severe hypoglycemia requiring treatment by emergency room admission within 6 months • Poor metabolic control requiring hospitalization within 6 months
Primary Endpoint	**Secondary Endpoints**
• Change in HbA1c from baseline to week 26	• Change in HbA1c from baseline to week 52 • Hypoglycemic event rates

- **Results:**
  - Baseline demographics were balanced between the groups, although there were slightly more elderly (≥ 65 years) and overweight (BMI ≥ 25 to < 30 kg/m^2) patients in the Admelog group. The mean age of the study population was 43 years, 8.7% of patients were ≥ 65 years old, and mean BMI at baseline was 26.0 kg/m^2.
  - Overall, 94.7% of patients completed the 26-week treatment period, and 90.9% completed the 52-week treatment period. A similar number of patients in each treatment group discontinued the study prematurely; the most common reason reason for withdrawal was "other," which included patient decision or consent withdrawal.
  - Admelog and Humalog demonstrated similar reductions in mean HbA1c from baseline to week 26; noninferiority of Admelog to Humalog was confirmed at the prespecified 0.3% margin (see Table 4). Additionally, fasting plasma glucose (FPG), 7-point self-measured plasma glucose (SMPG) profiles, and body weight changes from baseline were similar between treatment groups.
  - Rates of treatment-emergent adverse events (TEAEs) were comparable between the Admelog and Humalog groups (54.4% vs 55.5%, respectively); incidence of treatment-emergent anti-insulin antibody (AIA) responses was similar (22.6% vs 24.2%, respectively). Rates of hypoglycemia and severe hypoglycemia were also similar (see Table 4).

Table 4. Efficacy outcomes SORELLA 1

Outcomes	Admelog (n = 253)*	Humalog (n = 254)*
Mean HbA1c at baseline	8.08%	8.00%
LS mean change in HbA1c at 26 weeks	-0.42%	-0.47%
LS mean difference (95% CI)	0.06% (-0.084 to 0.197)	
LS mean change in HbA1c at 52 weeks	-0.22%	-0.30%
LS mean difference (95% CI)	0.07% (-0.084 to 0.232)	
	Admelog (n = 252)**	Humalog (n = 254)**
Any hypoglycemia during 52-week treatment period	250 (99.2%)	254 (100%)
Severe hypoglycemia during 52-week treatment period	34 (13.5%)	34 (13.4%)

Abbreviations: CI = confidence interval, LS = least squares
*intention-to-treat (ITT) population
** Safety population

- **Authors' conclusion:**
  - The results of this RCT in patients with T1DM also using insulin glargine U100 support similar efficacy and safety of Admelog to its reference drug Humalog.
- **Study Appraisal:**
  - **Study sponsorship:**
    - Sanofi
  - **Study rating:**
    - Fair
  - **Study strengths:**
    - The study used an appropriate comparator and had a safety extension.
  - **Study limitations:**
    - The study was OL.
    - No common insulin titration algorithm was used.

Study 2. Derwahl et al, *Diabetes Technol Ther.* 2018;20(2):160-170. SORELLA 2

Study Objective: Evaluate the safety, efficacy, and immunogenicity of Admelog vs Humalog in adult patients with T2DM treated with multiple daily injections, while using insulin glargine (Lantus) as basal insulin.	
Study Design, Follow-up	**Treatment Groups**
• 26-week, Phase 3, MC, OL, PG, RCT	• Admelog SC before meals with basal insulin glargine U100 (n = 253) • Humalog SC before meals with basal insulin glargine U100 (n = 252) • The starting doses of Admelog and Humalog were based on a unit-to-unit conversion from the patients' previous rapid-acting insulin dose. • Admelog and Humalog doses were titrated based on a 2-hr PPG goal of 120 to 160 mg/dL. Patients were instructed to self-adjust doses according to local guidelines. • Insulin glargine U100 was maintained at the pre-study dose and given once daily at the same time as used before study initiation. • The basal insulin fasting prebreakfast goal was between 80 to 130 mg/dL. There was no formal titration algorithm for basal insulin
Inclusion Criteria	**Exclusion Criteria**
• Adults with T2DM diagnosed for at least 12 months • HbA1c ≥ 6.5% and ≤ 10% • Treated with insulin glargine as basal insulin and Humalog or Novolog as mealtime insulin for at least 6 months	• BMI ≥ 40 kg/m^2 • Use of GLP-1 receptor agonists or other peptides or the use of CSII • History of severe hypoglycemia requiring treatment by emergency room admission within 6 months • Poor metabolic control requiring hospitalization within 6 months • Unstable proliferative diabetic retinopathy
Primary Endpoint	**Key Secondary Endpoint**
• Change in HbA1c from baseline to week 26	• Hypoglycemic event rates

- **Results:**
  - Baseline demographics were well balanced between the groups. Mean age was 62.5 years and more than 40% of the population was ≥ 65 years. The mean BMI was 32.2 kg/m^2, with most of the patients (93%) being overweight or obese. The mean duration of T2DM was 17.1 years and 19.8% had moderate renal impairment (estimated glomerular filtration rate [eGFR] ≥ 30 and < 60 mL/min/1.73m^2.
  - Overall, a similar number of patients in each group discontinued the study prematurely (9.9% in the Admelog group and 8.7% in the Humalog group); the most common reasons for discontinuation were "other reasons" and "adverse events".
  - Admelog and Humalog demonstrated similar reductions in mean HbA1c from baseline to week 26; noninferiority of

Admelog to Humalog was confirmed at the prespecified 0.3% margin (see Table 5). Additionally, FPG, 7-point SMPG profiles, and body weight changes from baseline were similar between treatment groups.
- Rates of hypoglycemia were similar between the groups (see Table 5). Severe hypoglycemia was rare, with 9 events reported in 6 patients in the Admelog group and 4 events reported in 4 patients in the Humalog group; the higher rate in the Admelog group was due to 1 patient who reported 4 events of severe hypoglycemia. Incidence of treatment-emergent AIA responses was similar between the Admelog and Humalog groups (24.5% vs 25.4%, respectively).

Table 5. Efficacy outcomes SORELLA 2

Outcomes	Admelog (n = 253)	Humalog (n = 252)
Mean HbA1c at baseline	7.99%	8.03%
LS mean change in HbA1c 26 weeks	-0.92%	-0.85%
LS mean difference (95% CI)	-0.07% (-0.215 to 0.067)	
Any hypoglycemia	68.4%	74.6%
Severe hypoglycemia	2.4%	1.6%

Abbreviations: CI = confidence interval, LS = least squares

- **Authors' conclusion:**
  - The results of this RCT in patients with T2DM also using insulin glargine U100 support similar efficacy and safety of Admelog to its reference drug Humalog.
- **Study Appraisal:**
  - **Study sponsorship:**
    - Sanofi
  - **Study rating:**
    - Fair
  - **Study strengths:**
    - The study used an appropriate comparator.
  - **Study limitations:**
    - The study was OL.
    - No common insulin titration algorithm was used.

<u>Afrezza (insulin human)</u>

Study 3a. Bode et al, *Diabetes Care*. 2015;38(12):2266-2273.
Study 3b. Rosenstock et al, *Diabetes Care*. 2015;38:2274-2281.

Study	Description
Study 3a: Afrezza vs Novolog in T1DM	• **Study Design:** ○ 24-week, Phase 3, MC, OL, PG, RCT (N = 351) ○ Adults with T1DM (HbA1c 7.5 to 10.0%) for at least 12 months ○ Patients were required to be nonsmokers for ≥ 6 months and have adequate baseline lung function tests • **Treatment Arms:** ○ Prandial Afrezza + basal insulin; prandial Novolog + basal insulin ○ Patients continued their pre-enrollment basal insulin • **Efficacy Results:** ○ Mean change in HbA1c in Afrezza patients (-0.21%) from baseline was noninferior to that in Novolog patients (-0.40%) from baseline. The between-group difference was 0.19%, satisfying the noninferiority margin of 0.4%. ○ More Novolog patients achieved HbA1c < 7.0% (30.7% vs 18.3%). ○ The mean daily dose of Afrezza increased throughout the randomized treatment phase (from 84.7 U at week 1 to 115.4 U at week 24). By contrast, in the Novolog group, the mean daily dose of Novolog showed only a slight increase (24.3 U at week 1 and 25.9 U at week 24). Additionally, doses of basal insulin used were higher in the Afrezza group than in the Novolog group. ○ The Afrezza arm experienced a slight weight loss (-0.4 kg) vs a gain (+0.9 kg) for Novolog patients (p = 0.0102). ○ Afrezza patients had a lower hypoglycemia event rate than Novolog patients (9.8 vs 14.0 events/patient-month; p < 0.0001). ○ Cough was the most frequent AE (31.6% with Afrezza vs 2.3% with Novolog), leading to discontinuation of 5.7% of patients. • **Authors' Conclusion:**

	○ In patients with T1DM receiving basal insulin, HbA1c reduction with Afrezza was noninferior to that of Novolog, with less hypoglycemia and less weight gain but increased incidence of cough.
Study 3b: Afrezza vs placebo in T2DM	▸ **Study Design:** ○ 24-week, Phase 3, MC, DB, PC, RCT (N = 353) ○ Adults with T2DM (HbA1c 7.5 to 10.0%) on metformin alone or 2 or more OADs ○ Patients were required to be nonsmokers for ≥ 6 months and have adequate baseline lung function tests ▸ **Treatment Arms:** ○ Prandial Afrezza or placebo as add-on therapy to baseline OAD regimen ▸ **Efficacy Results:** ○ From baseline to 24 weeks, Afrezza significantly reduced HbA1c by -0.8% vs -0.4% for placebo (treatment difference, -0.4%; 95% CI, -0.57 to -0.23; p < 0.0001). ○ Mean fasting BG was reduced more in the Afrezza arm, but the difference was not statistically significant (treatment difference, -7.42 mg/dL; 95% CI, -18.03 to 3.18; p = 0.1698). ○ Rates of hypoglycemia were higher in the Afrezza group vs placebo (67.8% vs 30.7%; p < 0.0001). Mild, transient dry cough was the most common AE and occurred similarly in both groups. ▸ **Authors' Conclusion:** ○ Prandial Afrezza added to 1 or more OADs in inadequately controlled T2DM is an effective treatment option.

<u>**Apidra (insulin glulisine)**</u>

Study 4a. Daily et al, *Diabetes Care.* 2004;27:2363-2368.
Study 4b. Dreyer et al, *Horm Metab Res.* 2005;37:702-707.
Study 4c. Rayman et al, *Diabetes Res Clin Pract.* 2007;76(2):304-312.

Study	Description
Study 4a: Apidra/Neutral Protamine Hagedorn (NPH) insulin vs regular insulin/ NPH insulin in T2DM	▸ **Study Design:** ○ 26-week, Phase 3, MC, OL, PG, RCT (N = 876) ○ Adults with T2DM (HbA1c 6.0 to 11.0%) on insulin therapy for ≥ 6 months ▸ **Treatment Arms:** ○ Apidra/NPH insulin SC twice daily; regular insulin/NPH insulin SC twice daily ○ Subjects were allowed to continue the same prestudy regimens of OADs ▸ **Efficacy Results:** ○ A slightly greater HbA1c reduction from baseline to 26 weeks was seen with Apidra vs regular insulin (-0.46% vs -0.30%; p = 0.0029). ○ BG values were lower with Apidra vs regular insulin at all treatment points of the 7-point SMBP, with statistical significance reached at 2 hours post-breakfast and 2 hours post-dinner (p < 0.05). ○ Symptomatic hypoglycemia and weight gain were comparable between the treatment groups. ▸ **Authors' Conclusion:** ○ Twice-daily Apidra with NPH insulin can provide small improvements in glycemic control compared with regular insulin in patients with T2DM who are already relatively well controlled on insulin ± OADs.
Study 4b: Apidra/insulin glargine vs Humalog/insulin glargine in T1DM	▸ **Study Design:** ○ 26-week, Phase 3, MC, OL, PG, RCT (N = 683) + 26-week safety extension ○ Adults with T1DM (HbA1c 6.0 to 11.0%) with BMI < 35 kg/m^2 ▸ **Treatment Arms:** ○ Apidra SC before meals/insulin glargine SC daily; Humalog SC before meals/insulin glargine SC daily ▸ **Efficacy Results:** ○ From baseline to 26 weeks, a similar reduction in mean HbA1c occurred in both groups (adjusted mean change from baseline -0.14% in both groups; p = 0.9329 for noninferiority). ○ SMBP were similar between the groups, with no between-group differences in terms of pre-prandial, bedtime, or nocturnal BG levels. ○ Basal insulin dose was relatively unchanged in the Apidra group (+ 0.12 U) but increased in the Humalog group (+1.82 U; p < 0.001 for between-group difference). The clinical relevance of this difference is unknown. ○ Rates of symptomatic hypoglycemia and TEAEs were similar between the groups.

	• **Authors' Conclusion:** ○ Apidra is as effective and well-tolerated as Humalog as part of basal-bolus therapy in combination with insulin glargine for the treatment of T1DM.
Study 4c: Apidra/NPH insulin vs regular insulin/NPH insulin in T2DM	• **Study Design:** ○ 26-week, Phase 3, MC, OL, PG, RCT (N = 890) ○ Adults with T2DM (HbA1c 6.0 to 11.0%) on insulin therapy for ≥ 6 months • **Treatment Arms:** ○ Apidra/NPH insulin SC twice daily; regular insulin/NPH insulin SC twice daily ○ Subjects were allowed to continue the same prestudy regimens of OADs (except for repaglinide, nateglinide, or glitazones) • **Efficacy Results:** ○ There were no differences in baseline to endpoint HbA1c reductions (Apidra -0.32% vs regular insulin -0.35%; 95% CI, -0.07 to 0.13; p = 0.5726). ○ Post-prandially, Apidra lowered BG more vs regular insulin at 2 hours (14.14 mmol/L vs 15.28 mmol/L; 95% CI, -1.87 to -0.40; p = 0.0025). ○ No between-group differences were seen in the frequency of symptomatic hypoglycemia; nocturnal hypoglycemia from Month 4 to treatment end was less frequent with Apidra vs regular insulin (9.1% vs 14.5%; p = 0.029). • **Authors' Conclusion:** ○ Apidra was noninferior to regular insulin in reducing HbA1c in T2DM. Apidra was superior in terms of post-prandial control and was associated with fewer nocturnal hypoglycemic episodes.

Fiasp (insulin aspart)

Study 5a. Russell-Jones et al, *Diabetes Care.* 2017;40:943-950. Onset 1
Study 5b. Mathieu C et al, *Diabetes Obes Metab.* 2018. [Epub ahead of print] Onset 1 safety extension

Study Objective: Evaluate the safety and efficacy of Fiasp vs Novolog in adults with T1DM.	
Study Design, Follow-up	**Treatment Groups**
• 26-week, Phase 3, MC, AC, PG, RCT ○ After an 8-week run-in period, patients were randomized to DB mealtime Fiasp or Novolog or OL postmeal Fiasp. • Additional 26-week OL treatment period to document safety	• Fiasp SC 0 to 2 minutes before each main meal (n = 381) • Novolog SC 0 to 2 minutes before each main meal (n = 380) • Fiasp SC 20 minutes after the start of a meal (n = 382) • Patients were optimized on basal insulin detemir during the 8-week run-in period. All subjects commenced mealtime Novolog at the start of the 8-week run-in period; after run-in, patients were randomized to receive their respective trial treatments. • Randomization was stratified in part by the method used by the subject for adjusting bolus insulin (carbohydrate counting or dosing algorithm). • After run-in, basal adjustments were only performed when required as judged by the investigator; dose frequency could not be changed.
Inclusion Criteria	**Exclusion Criteria**
• Adults (≥ 18 years old) with T1DM • Treated with basal-bolus insulin for ≥ 12 months prior to screening and treated with any regimen of insulin detemir or glargine for ≥ 4 months prior to screening • HbA1c of 7.0 to 9.5% • Body mass index (BMI) ≤ 35.0 kg/m^2	• Use of an antidiabetes drug other than insulin within 3 months prior to screening • Cardiovascular (CV) disease within 6 months prior to screening • Recurrent, severe hypoglycemia (> 1 event during the past 12 months) • Hypoglycemic unawareness as judged by the investigator • Hospitalization for diabetic ketoacidosis within 6 months prior to screening
Primary Endpoint	**Confirmatory Secondary Endpoints**
• Change from baseline in HbA1c after 26 weeks (noninferiority of mealtime Fiasp vs Novolog)	• Change from baseline in HbA1c after 26 weeks (noninferiority of postmeal Fiasp vs Novolog) • Change from baseline after 26 weeks of treatment in 2-hr

	PPG increment • Number of treatment-emergent severe or BG-confirmed hypoglycemic episodes (as defined according to the ADA classification or by a BG < 56 mg/dL with or without hypoglycemic symptoms) • Change from baseline in bodyweight after 26 weeks

- **Results:**
  - Baseline characteristics were similar among the 3 treatment arms; across the trial, median age was 44.4 years, median BMI was 26.7 kg/m^2, and median duration of diabetes was 19.9 years. Overall, 92.9% of patients completed the 26-week trial.
  - In regard to the effect on HbA1c from baseline, noninferiority of Fiasp, both mealtime and postmeal dosing, to mealtime Novolog was confirmed (see Table 6). The reduction in HbA1c was statistically significantly greater for mealtime Fiasp than Novolog, but superiority could not be confirmed as this was not part of the hierarchical testing procedure.
  - Mealtime Fiasp demonstrated a statistically significant change from baseline in 2-hr PPG increment vs Novolog (see Table 6). There were no significant differences between the groups in change from baseline in 3-hr or 4-hr PPG increments.
  - The mean body weight increase from baseline in all 3 treatment groups was < 1 kg over the 26-week period; there were no statistically significant differences between the groups.
  - There were no statistically significant differences in the overall rate of treatment-emergent severe or BG-confirmed hypoglycemic episodes among the groups (see Table 6). The rate of severe or BG-confirmed hypoglycemic episodes during the first hour after the start of a main meal was statistically significantly higher for mealtime Fiasp than for Novolog (RR, 1.48; 95% CI, 1.11 to 1.96; p < 0.0073); however, the number of episodes reported during this time period was a small fraction of the overall hypoglycemic episodes (~1 of 40).
  - Rates of treatment-emergent AEs (TEAEs) and serious AEs (SAEs) were comparable among the groups. Injection-site reactions occurred in 7, 9, and 3 patients in the Fiasp mealtime, postmeal, and Novolog groups, respectively; all were of mild or moderate severity.

Table 6. Efficacy outcomes Onset 1

	Fiasp mealtime (n = 381)	Novolog mealtime (n = 380)	Fiasp postmeal (n = 382)
Mean HbA1c at baseline	7.6%	7.6%	7.6%
Mean HbA1c at 26 weeks	7.3%	7.4%	7.5%
ETD (95% CI; p-value)	-0.15% (-0.23 to 0.07; p < 0.0001 for noninferiority)		
ETD (95% CI; p-value)		0.04% (-0.04 to 0.12; p < 0.0001 for noninferiority)	
Change from baseline in 2-hr PPG increment	-5.2 mg/dL	6.8 mg/dL	--
ETD (95% CI; p-value)	-12.01 mg/dL (-23.33 to -0.70; p = 0.0375 for superiority)		
ETD (95% CI; p-value)		5.32 mg/dL (-6.05 to 16.68; p = 0.93)	
Severe or BG-confirmed hypoglycemic episodes, no.	358 (92.7%)	370 (97.4%)	358 (95.0%)
RR (95% CI; p-value)	1.01 (0.88 to 1.15; p = 0.9191)		
RR (95% CI; p-value)		0.92 (0.81 to 1.06; p = 0.2435)	

Abbreviations: BG = blood glucose, CI = confidence interval, ETD = estimated treatment difference, PPG = post-prandial glucose, RR = rate ratio

  - Patients from the mealtime Fiasp and Novolog arms continued treatment for an additional 26 weeks. After 52 weeks, estimated mean changes from baseline in HbA1c levels were -0.08% for Fiasp and +0.01% for Novolog (ETD -0.10%; 95% CI, -0.19 to -0.00; p = 0.0424). There was no difference in rate of overall severe or BG-confirmed hypoglycemic episodes between the groups *(Mathieu et al 2018)*.
- **Authors' conclusion:**
  - In patients with T1DM on a basal-bolus insulin regimen, both mealtime and postmeal Fiasp were noninferior to mealtime Novolog regarding HbA1c change from baseline. Fiasp offered superior control of PPG excursions vs Novolog without increased risk of overall hypoglycemia.
- **Study Appraisal:**
  - **Study sponsorship:**
    - Novo Nordisk
  - **Study rating:**
    - Fair
  - **Study strengths:**

- All statistical analyses were based on the full analysis set (FAS).
- The study was DB (mealtime Fiasp and Novolog groups).

- **Study limitations:**
  - Confirmatory endpoints were tested using a hierarchical procedure. Because step 4 (number of treatment-emergent severe or BG-confirmed hypoglycemic episodes: superiority of mealtime Fiasp vs Novolog) was not confirmed, the stepwise testing procedure was stopped.
  - Baseline 1- to 4-hr PPG levels were assessed after a bolus dose of Novolog (0.1 units/kg) administered 0 to 2 minutes before a standardized mixed liquid meal test. The meal test was repeated at week 26, with patients administering the same bolus dose with their assigned treatment regimen. No adjustment was made for individual insulin-to-carbohydrate ratios and therefore the insulin dose was only an approximation of the patients' usual doses.

Study 6. Bowering et al, *Diabetes Care.* 2017;40:951-957. Onset 2

Study Objective: Evaluate the safety and efficacy of Fiasp vs Novolog in adults with T2DM receiving basal insulin and OADs.	
Study Design, Follow-up	**Treatment Groups**
• 26-week, Phase 3, MC, DB, AC, RCT ○ After an 8-week run-in period, patients were randomized to DB mealtime Fiasp or Novolog	• Fiasp SC 0 to 2 minutes before each main meal (n = 345) • Novolog SC 0 to 2 minutes before each main meal (n = 344) • During the 8-week run-in period, patients were optimized on basal insulin glargine; OADs (except for metformin) were discontinued. After run-in, patients were randomized to receive their respective trial treatments in addition to basal insulin glargine and metformin. • After randomization, bolus insulin dose adjustments were performed daily by the subject based on a titration guideline. • After run-in, basal adjustments were only performed when required as judged by the investigator; dose frequency could not be changed.
Inclusion Criteria	**Exclusion Criteria**

• Adults with T2DM
• Treated with basal insulin for ≥ 6 months prior to screening
• Treated with metformin (stable dose ≥ 1000 mg) alone or with an SFU, GLN, DPP-4 inhibitor, and/or an alpha-glucosidase inhibitor for ≥ 3 months prior to screening
  ○ Patients receiving metformin monotherapy were required to have an HbA1c of 7.0 to 9.5% at screening
  ○ Patients receiving metformin + additional OADs were required to have an HbA1c of 7.0 to 9.0%
• BMI ≤ 40 kg/m^2
	• Previous bolus insulin use (except for short-term use due to intermittent illness)
	• GLP-1 agonist and/or TZD use within 3 months prior to screening
	• CV disease within 6 months prior to screening
	• Recurrent, severe hypoglycemia (> 1 event during the past 12 months)
	• Hypoglycemic unawareness as judged by the investigator
	• Hospitalization for diabetic ketoacidosis within 6 months prior to screening

Primary Endpoint	**Confirmatory Secondary Endpoints**
• Change from baseline in HbA1c after 26 weeks	• Change from baseline after 26 weeks of treatment in 2-hr PPG increment • Number of treatment-emergent severe or BG-confirmed hypoglycemic episodes (as defined according to the ADA classification or by a BG < 56 mg/dL with or without hypoglycemic symptoms) • Change from baseline in bodyweight after 26 weeks

- **Results:**
  - Baseline characteristics were similar between the treatment arms. Across the trial, median age was 59.5 years, median BMI was 31.2 kg/m^2, and median duration of diabetes was 12.7 years. At baseline, 53.8% of patients were on basal insulin + 1 OAD, 43.7% were on basal insulin + 2 OADs, and 2.5% were on basal insulin + > 2 OADs. Overall, 88% of patients completed the trial.
  - Noninferiority of Fiasp to Novolog was confirmed in regard to effect on HbA1c (see Table 7). Superiority of Fiasp vs

Novolog in 2-hr PPG increment lowering was not confirmed; however, the estimated change from baseline in 1-hr PPG increment was -38.5 mg/dL for Fiasp and -27.9 mg/dL for Novolog (ETD -10.63 mg/dL; 95% CI, -19.56 to -1.69; p < 0.0198). There was no statistical difference in ETD for change from baseline in 3-hr or 4-hr PPG increments.
- In both groups, body weight increased by ~2.7 kg over the trial period.
- The difference in overall rate of severe or BG-confirmed hypoglycemia was not statistically significant between treatment groups (see Table 7). For the interval 0 to 2 hours after meals, a statistically significantly higher rate of meal-related hypoglycemia was reported for Fiasp (RR, 1.60; 95% CI, 1.13 to 2.27; p = 0.0082).
- The rate of TEAEs was similar between groups; most were mild or moderate in severity.

Table 7. Efficacy outcomes Onset 2

	Fiasp (n = 345)	Novolog (n = 344)
Mean HbA1c at baseline	8.0%	7.9%
Mean HbA1c at 26 weeks	6.6%	6.6%
ETD (95% CI; p-value)	-0.02% (-0.15 to 0.10; p < 0.0001 for noninferiority)	
Change from baseline in 2-hr PPG increment	-58.3 mg/dL	-51.8 mg/dL
ETD (95% CI; p-value)	-6.57 mg/dL (-14.54 to 1.41; p = NS for superiority)	
Severe or BG-confirmed hypoglycemic episodes, no.	262 (76.8%)	250 (73.3%)
RR (95% CI; p-value)	1.09 (0.88 to 1.36; p = NS for superiority)	

Abbreviations: BG = blood glucose, CI = confidence interval, ETD = estimated treatment difference, NS = not significant, PPG = post-prandial glucose, RR = rate ratio

- **Authors' conclusion:**
  - In adults with T2DM inadequately controlled on basal insulin and OADs, insulin intensification with Fiasp or Novolog improved overall glycemic and PPG control. Overall hypoglycemia rates were similar between groups, with an increase in hypoglycemia rates during the 0 to 2-hr postmeal interval with Fiasp. Both Fiasp and Novolog are effective, well-tolerated treatment options for patients requiring mealtime insulin.
- **Study Appraisal:**
  - **Study sponsorship:**
    - Novo Nordisk
  - **Study rating:**
    - Fair
  - **Study strengths:**
    - All statistical analyses were based on the FAS.
    - The study was DB.
  - **Study limitations:**
    - Confirmatory endpoints were tested using a hierarchical procedure. Because step 2 (change from baseline in 2-hr PPG increment: superiority of Fiasp vs Novolog) was not confirmed, the stepwise testing procedure was stopped.
    - Baseline 1- to 4-hr PPG levels were assessed after a bolus dose of Novolog (0.1 units/kg) administered 0 to 2 minutes before a standardized mixed liquid meal test. The meal test was repeated at week 26, with patients administering the same bolus dose with their assigned treatment regimen. No adjustment was made for individual insulin-to-carbohydrate ratios and therefore the insulin dose was only an approximation of the patients' usual doses.
    - The initiation of 3 bolus insulin doses simultaneously in patients with T2DM is not representative of real world clinical practice.

Study 7. Rodbard et al, *Diabetes Obes Metab.* 2017;19:1389-1396. Onset 3

Study Objective: To evaluate the safety and efficacy of adding Fiasp to basal insulin therapy vs basal insulin alone, both in combination with metformin, in patients with inadequately controlled T2DM.

Study Design, Follow-up	Treatment Groups
• 18-week, Phase 3, MC, OL, PG, RCT	• Fiasp SC before each main meal + basal insulin (n = 116) • Basal insulin (n = 120) • Patients continued their basal insulin of choice from baseline (insulin glargine, insulin detemir, or NPH insulin). • During the 8-week run-in period, patients were optimized on basal insulin; OADs (except for metformin) were discontinued. After run-in, patients were randomized to continue with basal insulin + metformin, or mealtime Fiasp + basal insulin + metformin.

	• After randomization, bolus insulin dose adjustments were performed daily by the subject based on a titration guideline. • After run-in, the basal insulin dose was adjusted at the investigator's discretion.
Inclusion Criteria	**Exclusion Criteria**

• Adults with T2DM
• Treated with basal insulin and metformin ≥ 1000 mg with or without other OADs for ≥ 3 months prior to screening
  ○ Patients receiving metformin monotherapy were required to have an HbA1c of 7.5 to 9.5% at screening
  ○ Patients receiving metformin + additional OADs were required to have an HbA1c of 7.5 to 9.0%
• BMI ≤ 40 kg/m^2
	• Previous bolus insulin use (except for short-term use due to intermittent illness)
	• GLP-1 agonist and/or TZD use within 3 months prior to screening
	• CV disease within 6 months prior to screening
	• Recurrent, severe hypoglycemia or hypoglycemia unawareness

Primary Endpoint	**Key Secondary Endpoints**
• Change from baseline in HbA1c after 18 weeks	• Proportion of patients achieving HbA1c targets of < 7.0% • Change from baseline in overall 2-hr PPG increment (all meals) • Number of treatment-emergent severe or BG-confirmed hypoglycemic episodes (as defined according to the ADA classification or by a BG < 56 mg/dL with or without hypoglycemic symptoms)

- **Results:**
  - Baseline characteristics were well-matched between the groups. Mean age was 57.4 years, mean BMI was 30.8 kg/m^2, and duration of diabetes was 10.9 years for the Fiasp + basal group and 11.8 years for the basal group. An equivalent proportion of patients utilized insulin glargine, insulin detemir, and NPH insulin as their basal insulin in both groups. Overall, 94.1% of patients completed the trial.
  - Superiority of Fiasp + basal insulin over basal insulin alone was confirmed in regard to HbA1c reduction and the proportion of patients achieving an HbA1c < 7.0% (see Table 8).
  - Mean body weight increased by 1.8 kg in the Fiasp + basal insulin group and 0.2 kg in the basal only group (ETD, 1.66; 95% CI, 0.89 to 2.43; p < 0.0001).
  - Severe or BG-confirmed hypoglycemic episodes occurred at a significantly higher rate in the Fiasp + basal insulin group (see Table 8).
  - Overall, TEAEs were reported in 40.9% of patients in the Fiasp + basal insulin group and 51.7% of patients in the basal only group; most TEAEs were mild or moderate in severity.

Table 8. Efficacy outcomes Onset 3

	Fiasp + basal insulin (n = 116)	Basal insulin (n = 120)
HbA1c at baseline	7.9%	7.9%
HbA1c at 18 weeks	6.8%	7.7%
ETD (95% CI; p-value)	-0.94% (-1.17 to -0.72; p < 0.0001 for superiority)	
Patients achieving HbA1c < 7.0% at 18 weeks	60.3%	18.3%
OR (95% CI; p-value)	9.31 (4.72 to 18.33; p < 0.0001)	
Change from baseline in 2-hr PPG increment	-26 mg/dL	-9 mg/dL
ETD (95% CI; p-value)	-20.5 mg/dL (-27.1 to -13.8; p < 0.0001)	
Severe or BG-confirmed hypoglycemic episodes, no.	67 (58.3%)	30 (25.0%)
RR (95% CI; p-value)	8.24 (4.93 to 13.76; p < 0.0001)	

Abbreviations: BG = blood glucose, CI = confidence interval, ETD = estimated treatment difference, OR = odds ratio, PPG = post-prandial glucose, RR = rate ratio

- **Authors' conclusion:**
  - In patients with T2DM, Fiasp in a basal-bolus regimen provided superior glycemic control as compared with basal-only insulin, but with an increase in the frequency of hypoglycemia and modest weight gain.
- **Study Appraisal:**
  - **Study sponsorship:**

- Novo Nordisk
- Study rating:
  - Fair to Poor
- **Study strengths:**
  - All statistical analyses were based on the FAS.
- **Study limitations:**
  - The study was of short duration.
  - The study was OL with no active comparator; therefore, no conclusion can be drawn regarding the benefit of Fiasp vs other mealtime insulins.
  - The initiation of 3 bolus insulin doses simultaneously in patients with T2DM is not representative of real world clinical practice.

Comparative Efficacy and Meta-Analyses

Study 8a. van Bon et al, *Diabetes Technol Ther.* 2011;13(6):607-614.
Study 8b. Plank et al, *Arch Intern Med.* 2005;165:1337-1344.
Study 8c. Fullerton et al, *Cochrane Database Syst Rev.* 2016;(6):CD012161.

Study	Description
Study 8a: Apidra (GLU) vs Humalog (LIS) and Novolog (ASP) for CSII	▪ **Study Design:** ○ 39-week, MC, OL, 3-way XO, RCT (N = 256) ○ Adults with T1DM (HbA1c < 8.5%) treated with insulin for ≥ 2 years and CSII for ≥ 6 months ○ The study was designed to demonstrate superiority of GLU over ASP or LIS in rates of unexplained hyperglycemia and/or perceived infusion set occlusion. A prespecified p-value of 0.025 was considered significant to correct for multiple testing. ▪ **Treatment Arms:** ○ Patients were randomized to 1 of 3 treatment orders: GLU-ASP-LIS, ASP-LIS-GLU, LIS-GLU-ASP ○ Each insulin was used for 13 weeks. ▪ **Efficacy Results:** ○ The percentage of patients with unexplained hyperglycemia and/or perceived infusion set occlusion was not significantly different between GLU and ASP (68.4% vs 62.1%; $p = 0.04$) or GLU and LIS (68.4% vs 61.3%; $p = 0.03$). ○ No differences were seen in HbA1c, severe hypoglycemia, or symptomatic ketoacidosis. ○ The overall rate of hypoglycemia (BG < 70 mg/dL) per patient-year was significantly different between GLU and ASP (73.84 vs 65.01; $p = 0.008$) and GLU and LIS (73.84 vs 62.69; $p < 0.001$). ▪ **Authors' Conclusion:** ○ GLU was not superior to ASP and LIS in CSII use with respect to unexplained hyperglycemia and/or perceived catheter set occlusion. GLU was associated with a higher frequency of symptomatic hypoglycemia, possibly because of slight overdosing, as previous trials have suggested lower insulin requirements when GLU is initiated in T1DM.
Study 8b: SR/MA of rapid-acting insulins (Humalog and Novolog) vs regular insulin	▪ **Study Design:** ○ 42 RCTs (N = 7933 patients) assessing the effects of rapid-acting insulins vs regular insulin in patients with T1DM (n = 5925), T2DM (n = 1901), or gestational diabetes (n = 107) ▪ **Efficacy Results:** ○ *HbA1c* ▪ In T1DM, the weighted mean difference of HbA1c values was estimated to be -0.12% (95% CI, -0.17 to -0.07%) in favor of rapid-acting insulins vs regular insulin. Heterogeneity was non-significant ($p = 0.06$). ▪ In T2DM, the weighted mean difference of HbA1c values was estimated to be -0.02% (95% CI, -0.10 to 0.07) between rapid-acting insulins and regular insulin. Similar results were found in studies with children and adolescents with T1DM and in gestational diabetes. ○ *Hypoglycemia* ▪ In T1DM, the standardized mean difference of overall mean hypoglycemic episodes per patient per month was -0.05 (95% CI, -0.22 to 0.11) for rapid-acting insulins vs regular insulin. In the included studies, distinct heterogeneity was observed ($p < 0.001$). ▪ In T2DM, the standardized mean difference of overall mean hypoglycemic episodes per patient per month was -0.04 (95% CI, -0.12 to 0.04; heterogeneity: $p = 0.74$) for rapid-acting insulins vs regular insulin. ▪ **Authors' Conclusion:**

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	○ In patients with T1DM, a minor benefit to HbA1c values was seen with the rapid-acting insulins vs regular insulin. No benefit was identified in patients with T2DM or gestational diabetes.
Study 8c: Cochrane Review: rapid-acting insulins vs regular insulins in T1DM	▪ **Study Design:** ○ SR of 9 RCTs with an intervention duration of at least 24 weeks that compared rapid-acting insulins with regular insulins in the treatment of non-pregnant adults with T1DM (N = 2693) ○ Of the included trials, 6 were of insulin lispro (Humalog) vs regular insulin and 3 were of insulin aspart (Novolog) vs regular insulin. None of the included trials used insulin glulisine (Apidra). ▪ **Efficacy Results:** ○ The mean difference in HbA1c was -0.15% (95% CI, -0.2 to -0.1%; $p < 0.00001$; 9 trials, low quality evidence) in favor of rapid-acting insulins. ○ There were no substantial differences in rates of overall hypoglycemia between the groups. The comparison of the risk of severe hypoglycemia between the 2 treatments showed an OR of 0.89 (95% CI, 0.71 to 1.12; $p = 0.31$; 7 trials, very low quality evidence). ○ In terms of nocturnal severe hypoglycemia, 2 trials reported statistically significant effects in favor of insulin aspart; however, due to inconsistent reporting, the validity of the results remains questionable. ▪ **Authors' Conclusion:** ○ The analysis suggests only a minor benefit of rapid-acting insulins on BG control in patients with T1DM; however, long-term efficacy and safety data are needed to draw conclusions on long-term patient-relevant outcomes such as all-cause mortality or diabetic complications.

CLINICAL GUIDELINES

- **American Diabetes Association (ADA): Standards of Medical Care in Diabetes** *(2018)* (see Appendix for levels of evidence)
  - HbA1c goals
    - A reasonable HbA1c goal for many nonpregnant adults is < 7%. (A)
    - Providers might reasonably suggest more stringent HbA1c goals (such as 6.5%) for selected patients if this can be achieved without significant hypoglycemia or other AEs of treatment. Appropriate patients might include those with short duration of diabetes, T2DM treated with lifestyle changes or metformin only, long life expectancy, or no significant cardiovascular disease (CVD). (C)
    - Less stringent HbA1c goals (such as < 8%) may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, or long-standing diabetes in whom the general goal is difficult to attain despite diabetes self-management education, appropriate glucose monitoring, and effective doses of multiple glucose-lowering agents, including insulin. (B)
  - Pharmacological therapy for T1DM:
    - Most people with T1DM should be treated with multiple-dose injections of basal and prandial insulin or CSII. (A)
    - Consideration should be given to educating patients on matching prandial insulin dose to carbohydrate intake, premeal BG, and anticipated physical activity. (E)
    - Most patients should use rapid-acting insulin analogs to reduce hypoglycemia risk. (A)
      - Rapid-acting inhaled insulin was shown to be noninferior to insulin aspart for HbA1c lowering, with less hypoglycemia observed; however the mean HbA1c reduction with insulin aspart was greater and more patients in the insulin aspart group achieved HbA1c goals of ≤ 7.0%. Because inhaled insulin cartridges are only available in 4-, 8-, and 12-unit doses, limited dosing increments to fine-tune prandial insulin doses in T1DM are a potential limitation.
    - Individuals who have been successfully using CSII should have continued access after they turn 65 years of age. (E)
  - Pharmacological therapy for T2DM:
    - Metformin (if not contraindicated and if tolerated) is the preferred initial pharmacological agent for T2DM. (A)
    - Metformin should be continued when used in combination with other agents, including insulin, if not contraindicated and if tolerated. (A)
    - Initiation of insulin therapy (with or without additional agents) should be considered in patients with newly diagnosed T2DM who are symptomatic and/or have elevated BG levels (≥ 300 mg/dL) and/or HbA1c (≥ 10%). (E)
    - Initiation of dual therapy should be considered in patients with newly diagnosed T2DM who have HbA1c ≥ 9%. (E)
    - For patients with T2DM who are not achieving glycemic goals, drug intensification, including consideration of insulin therapy, should not be delayed. (B)
    - In patients without atherosclerotic cardiovascular disease (ASCVD), if monotherapy or dual therapy does not achieve or maintain the HbA1c target over 3 months, an additional antihyperglycemic agent should be added based on drug-specific and patient factors. (A)
    - In patients with T2DM and established ASCVD, antihyperglycemic therapy should begin with lifestyle management and metformin and subsequently incorporate an agent proven to reduce major adverse cardiovascular events

(MACE) and cardiovascular (CV) mortality (currently empagliflozin and liraglutide), after consideration of drug-specific and patient factors. (A)
- In patients with T2DM and established ASCVD, after lifestyle management and metformin, the antihyperglycemic agent canagliflozin may be considered to reduce MACE, based on drug-specific and patient factors. (C)
- A patient-centered approach should be used to guide the choice of pharmacological agents. Considerations include efficacy, cost, potential AEs, impact on weight, hypoglycemia risk, history of ASCVD, renal effects, route of administration, and patient preferences. (E)

- Treatment Algorithm:
  - At diagnosis, lifestyle management should be initiated; the HbA1c target should be set; and pharmacologic therapy based on HbA1c should be initiated:
    - HbA1c < 9%: Consider Monotherapy.
    - HbA1c ≥ 9%: Consider Dual Therapy.
    - HbA1c ≥ 10%, BG ≥ 300 mg/dL, or patient is markedly symptomatic: Consider Combination Injectable Therapy.
- Monotherapy: Lifestyle Management + Metformin
  - Metformin should be initiated if there are no contraindications.
  - If the patient is at the target HbA1c after 3 months of monotherapy, the HbA1c should be monitored every 3 to 6 months. If the patient is not at target after 3 months, Dual Therapy should be considered.
- Dual therapy: Lifestyle Management + Metformin + Additional Agent
  - If the patient has ASCVD, an agent proven to reduce MACE and/or CV mortality should be added. If the patient does not have ASCVD, a second agent should be added after consideration of drug-specific effects and patient factors.
  - If the patient is at the target HbA1c after 3 months of monotherapy, the HbA1c should be monitored every 3 to 6 months. If the patient is not at target after 3 months, medication-taking behavior should be assessed and Triple Therapy should be considered.
- Triple therapy: Lifestyle Management + Metformin + 2 Additional Agents
  - A third agent should be added based on drug-specific effects and patient factors.
  - If the patient is at the target HbA1c after 3 months of monotherapy, the HbA1c should be monitored every 3 to 6 months. If the patient is not at target after 3 months, medication-taking behavior should be assessed and Combination Injectable Therapy should be considered.
- Combination injectable therapy:
  - Insulin therapy may be initiated in patients with an HbA1c ≥ 10%, BG ≥ 300 mg/dL, or in patients who are markedly symptomatic. If the HbA1c is not controlled, the following combination injectable therapy escalations may be considered:
  - Adding 1 rapid-acting insulin injection before the largest meal; adding a GLP-1 receptor agonist; or changing to premixed insulin 2 times daily (before breakfast and dinner). If goals are not met, an alternative insulin regimen may be considered.
    - Rapid-acting insulin analogs are preferred due to their prompt onset of action after dosing.
  - If HbA1c is not controlled from adding 1 rapid-acting insulin injection, adding ≥ 2 rapid-acting insulin injections before meals (basal-bolus) may be considered. If HbA1c is not controlled by premixed insulin twice daily, changing to a premixed analog insulin 3 times daily (breakfast, lunch, and dinner) may be considered.

- **American Association of Clinical Endocrinologists (AACE)/American College of Endocrinology (ACE) - Consensus Statement on the Comprehensive Type 2 Diabetes Management Algorithm (2018 Executive Summary)** (*Garber et al 2018*)
  - Lifestyle optimization is essential for all patients with diabetes.
  - The HbA1c target should be individualized based on numerous factors, such as age, life expectancy, comorbid conditions, duration of diabetes, risk of hypoglycemia or adverse consequences from hypoglycemia, patient motivation, and adherence. An HbA1c level of ≤ 6.5% is considered optimal if it can be achieved in a safe and affordable manner, but higher targets may be appropriate for certain individuals and may change for a given individual over time.
  - Glycemic control targets include fasting and post-prandial glucose as determined by self-monitoring of BG.
  - The choice of diabetes therapies must be individualized based on attributes specific to both patients and the medications themselves. Medication attributes include antihyperglycemic efficacy, mechanism of action, risk of inducing hypoglycemia, risk of weight gain, other AEs, tolerability, ease of use, likely adherence, cost, and safety in heart, kidney, or liver disease.
  - Minimizing risk of both severe and nonsevere hypoglycemia is a priority. Minimizing risk of weight gain is also a priority.
  - The treatment algorithm stratifies choice of therapies based on initial HbA1c level. It provides guidance as to what therapies to initiate and add but respects individual circumstances that could lead to different choices.
    - The algorithm includes every FDA-approved class of medications for T2DM (as of December 2016).

- Combination therapy is usually required and should involve agents with complementary mechanisms of action. Comprehensive management includes lipid and blood pressure therapies and treatment of related comorbidities.
- The therapeutic regimen should be as simple as possible to optimize adherence.
- Therapy must be evaluated frequently (eg, every 3 months) until the patient is stable, using multiple criteria (eg, HbA1c, self-monitoring of BG records, lipid and blood pressure levels, hypoglycemia events, AEs).
- Pharmacotherapy for T2DM:
  - In patients with recent-onset T2DM or mild hyperglycemia (HbA1c < 7.5%), lifestyle therapy plus antihyperglycemic monotherapy (preferably with metformin) is recommended. Acceptable alternatives to metformin include a GLP-1 receptor agonist, SGLT-2 inhibitor, DPP-4 inhibitor, and TZD. Alpha-glucosidase inhibitors and SFUs/GLNs may also be appropriate as monotherapy for select patients.
    - A TZD, SFU, or GLN should be used with caution due to their AE profiles.
    - The order of agents listed suggests a hierarchy of recommended usage.
  - If monotherapy fails to achieve the HbA1c goal in 3 months or the patient presents with an HbA1c ≥ 7.5%, then dual therapy should be started by adding 1 of the following agents to metformin (or other first-line agent): GLP-1 receptor agonist, SGLT-2 inhibitor, DPP-4 inhibitor, TZD, basal insulin, colesevelam, bromocriptine quick release (QR), alpha-glucosidase inhibitor, or SFU/GLN.
    - TZDs, basal insulin, SFUs, and GLNs should be used with caution due to their AE profiles.
    - The order of agents listed suggests a hierarchy of recommended usage.
  - If dual therapy does not achieve the HbA1c goal in 3 months, then triple therapy should be started by adding 1 of the following agents to metformin (or other first-line agent) plus a second-line agent: GLP-1 receptor agonist, SGLT-2 inhibitor, TZD, basal insulin, DPP-4 inhibitor, colesevelam, bromocriptine QR, alpha-glucosidase inhibitor, or SFU/GLN.
    - TZDs, basal insulin, SFUs, and GLNs should be used with caution due to their AE profiles.
    - The order of agents listed suggests a hierarchy of recommended usage.
    - Patients taking 2 oral antihyperglycemic agents who have an HbA1c > 8.0% and/or long-standing T2DM are unlikely to reach their target HbA1c with a third oral antihyperglycemic agent. A GLP-1 receptor agonist as the third agent may successfully lower glycemia, but eventually many patients will still require insulin. In such cases, a single daily dose of basal insulin should be added to the regimen.
  - If triple therapy fails to achieve the HbA1c goal in 3 months, then the patient should proceed to or intensify insulin therapy.
  - In patients with an HbA1c > 9.0%, dual therapy or triple therapy is recommended if the patient is asymptomatic. If the patient is symptomatic, insulin therapy alone or in combination with other agents is recommended.

SAFETY

- **Contraindications**

  Class Contraindications
  - During episodes of hypoglycemia
  - Hypersensitivity to the active ingredient or any of the excipients in the rapid-acting insulins

  Afrezza Contraindications
  - Chronic lung disease, such as asthma, or COPD
- **Warnings/precautions**
  - **Boxed warning: Afrezza: Risk of acute bronchospasm in patients with chronic lung disease**
    - Acute bronchospasm has been observed in patients with asthma and COPD using Afrezza. Before initiating Afrezza, a detailed medical history, physical examination, and spirometry (forced expiratory volume in 1 second [FEV_1]) should be performed to identify potential lung disease in all patients.
  - Insulin pens should never be shared, even if the needle is changed, due to the risk for transmission of blood-borne pathogens.
  - Hyper- or hypoglycemia with changes in insulin regimen
    - Doses of insulin should be changed under close medical supervision and the frequency of BG monitoring increased to minimize the risk of hyper- or hypoglycemia.
  - Hypoglycemia
    - Monitoring should be increased with changes to insulin dosage, concomitant glucose lowering agents, meal patterns, physical activity, and in patients with hypoglycemia unawareness, renal, or hepatic impairment.
  - Hypoglycemia due to medication errors
    - Patients should be informed to check insulin labels before injecting as accidental mix-ups between insulin products can occur.
  - Hypokalemia
    - Hypokalemia may be life-threatening and potassium levels should be monitored and treated, if indicated, in patients at risk for hypokalemia.
  - Hypersensitivity reactions

  - Severe, life-threatening, generalized allergy, including anaphylaxis can occur.
- Fluid retention and heart failure with concomitant use of TZDs
  - Patients should be monitored for signs and symptoms of heart failure, and a dose reduction or discontinuation should be considered if heart failure occurs.
- Acute bronchospasm/decline in pulmonary function (Afrezza)
  - Acute bronchospasm has been observed in patients with asthma and COPD. Pulmonary function should be assessed before initiating, after 6 months of therapy, and annually, even in the absence of pulmonary symptoms.
- Lung cancer (Afrezza)
  - Afrezza should not be used in patients with active lung cancer. In patients with a history of lung cancer or at risk for lung cancer, the benefit of Afrezza use should outweigh this potential risk.

- **Adverse effects**
  - Common AEs for the injectable rapid-acting insulins include hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, and rash.
  - Common AEs for Afrezza (≥ 2%) include hypoglycemia, cough, and throat pain or irritation.
- **Drug Interactions**

Table 9. Significant drug interactions for rapid-acting insulins

Precipitant Drug	Object Drug		Description of Effects
Antidiabetic agents, angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor blocking (ARB) agents, disopyramide, fibrates, fluoxetine, monoamine oxidase inhibitors, pentoxifylline, pramlintide, propoxyphene, salicylates, somatostatin analogs (eg, octreotide), and sulfonamide antibiotics	rapid-acting insulins	↑	Concomitant use increases the risk of hypoglycemia. Dose reductions and increased glucose monitoring may be required
Atypical antipsychotics (eg, olanzapine and clozapine), corticosteroids, danazol, diuretics, estrogens, glucagon, isoniazid, niacin, oral contraceptives, phenothiazines, progestogens (eg, in oral contraceptives), protease inhibitors, somatropin, sympathomimetic agents (eg, albuterol, epinephrine, terbutaline), and thyroid hormones	rapid-acting insulins	↓	Concomitant use decreases BG lowering effects of rapid-acting insulins. Dose increases and increased glucose monitoring may be required.
Alcohol, beta-blockers, clonidine, and lithium salts. Pentamidine may cause hypoglycemia, which may sometimes be followed by hyperglycemia.	rapid-acting insulins	↔	Concomitant use may increase or decrease the BG lowering effects of rapid-acting insulins. Dose increases and increased glucose monitoring may be required.
Beta-blockers, clonidine, guanethidine, and reserpine	rapid-acting insulins	↔	Concomitant use may blunt the signs and symptoms of hypoglycemia. Increased glucose monitoring may be required.

↑ = Object drug increased. ↓ = Object drug decreased. ↔ = Undetermined clinical effect.

DOSAGE AND ADMINISTRATION

General Dosing Considerations

- The dosage of rapid-acting insulins should be individualized based on the patient's metabolic needs, BG monitoring results, and glycemic control goal.
- Dose adjustments may be needed when switching from another insulin, with changes in physical activity, changes in concomitant medications, changes in meal patterns, changes in renal or hepatic function, or during acute illness to minimize the risk of hypo- or hyperglycemia.
- Injection sites (abdominal wall, thigh, upper arm, or buttocks) should be rotated within the same region from one injection to the next to reduce the risk of lipodystrophy.
- Rapid-acting insulins given by SC injection should generally be used in regimens with intermediate or long-acting insulin.
- For rapid-acting insulins approved for CSII use, product- and pump-specific instructions should be followed.
- Rapid-acting insulins should be administered by IV infusion only under medical supervision with close monitoring of BG and potassium levels to avoid hypoglycemia and hypokalemia.

Table 10. Dosing of rapid-acting insulins

Drug	Approved Routes of Administration	Dosing
Admelog (insulin lispro)	SC, IV, CSII	SC: administer within 15 minutes before a meal or immediately after a meal

		IV: dilute to concentrations from 0.1 unit/mL to 1 unit/mL in 0.9% sodium chloride
Afrezza (insulin human)	Inhalation	Starting mealtime dose: *Insulin naïve:* 4 units at each meal *Using SC prandial insulin:* determine the appropriate Afrezza dose by using the conversion chart provided in the prescribing information. For Afrezza doses exceeding 12 units, inhalations from multiple cartridges are necessary
Apidra (insulin glulisine)	SC, IV, CSII	SC: administer within 15 minutes before a meal or within 20 minutes after starting a meal IV: dilute to concentrations from 0.05 unit/mL to 1 unit/mL in 0.9% sodium chloride
Fiasp (insulin aspart)	SC, IV	SC: administer at the start of a meal or within 20 minutes after starting a meal IV: dilute to concentrations from 0.5 unit/mL to 1 unit/mL in 0.9% sodium chloride or 5% dextrose
Humalog (insulin lispro)	SC (U100, U200), IV (U100), CSII (U100)	SC (U100, U200): administer within 15 minutes before a meal or immediately after a meal IV (U100): dilute to concentrations from 0.1 unit/mL to 1 unit/mL in 0.9% sodium chloride
Novolog (insulin aspart)	SC, IV, CSII	SC: administer within 5 to 10 minutes before a meal IV: dilute to concentrations from 0.05 unit/mL to 1 unit/mL in 0.9% sodium chloride

Abbreviations: CSII = continuous subcutaneous insulin infusion, IV = intravenous, SC = subcutaneous

SPECIFIC POPULATIONS

- **Geriatrics**
  - In elderly patients, caution should be taken with initial insulin dosing and subsequent dose changes to avoid hypoglycemic reactions.
- **Pediatrics**
  - Admelog, Humalog, Apidra, and Novolog are approved for use in pediatric patients.
    - Admelog and Humalog have not been studied in pediatric patients with T1DM < 3 years of age or in pediatric patients with T2DM.
    - Apidra has not been studied in pediatric patients with T1DM < 4 years of age or in pediatric patients with T2DM.
    - Novolog has not been studied in pediatric patients with T1DM < 2 years of age or in pediatric patients with T2DM.
- **Renal dysfunction**
  - Patients with renal impairment may be at increased risk of hypoglycemia and may require more frequent insulin dose adjustment and more frequent BG monitoring.
- **Hepatic dysfunction**
  - Patients with hepatic impairment may be at increased risk of hypoglycemia and may require more frequent insulin dose adjustment and more frequent BG monitoring.
- **Pregnancy and nursing**
  - Humalog and Novolog are Pregnancy Category B (no evidence of risk in studies); Apidra is Pregnancy Category C (risk cannot be ruled out; either studies in animals have revealed adverse effects on the fetus and there are no controlled studies in women or studies in women and animals are not available).
  - Admelog, Afrezza, and Fiasp are uncategorized in accordance with the FDA's Pregnancy and Lactation Labeling Rule (PLLR). Limited data available in pregnant women are insufficient to determine a drug-associated risk of adverse developmental outcomes.

CONSULTANT: PC, M.D. (Endocrinology)

- **Consultant's Comments:**
  - The injectable rapid-acting insulin analogs are more similar than they are different. In practice, the consultant uses them interchangeably and has not noticed a difference in terms of efficacy or safety.
  - The consultant has limited experience with Fiasp. It may be useful for patients who need a faster onset of action, but the benefit remains unclear.
  - The SORELLA trials evaluating Admelog were relatively standard. The outcomes, populations, and duration were adequate to show nonferiority of Admelog to Humalog. SORELLA 1 had an extended period to look for antibodies as

well.
- Admelog will likely become clinically interchangeable with Humalog.
- Afrezza has been available for several years, but utilization is low. Generally, patients do not mind daily injections with the available pen devices. One niche may be for truck drivers who have T2DM as they are not allowed to use injectables. Afrezza could get around this issue while still providing similar efficacy to insulin.
- In terms of efficacy, Afrezza is probably similar to the other rapid-acting insulins, but safety is very different. It cannot be used in patients with pulmonary issues, and pulmonary function needs to be monitored long-term.

- **Disclosure of financial relationships:**
  - No potential conflicts of interest identified

CONSULTANT: EK, M.D. (Endocrinology)

- **Consultant's Comments:**
  - Given the impact of PPG on HbA1c as well as concerns with mealtime glucose excursions on vascular health, there has been great interest over recent years in more closely approximating true insulin response physiology. Despite pharmacologic advances which have reduced onset and peak times, we still have not reproduced finely tuned mealtime insulin effects. In addition, application of rapid-acting insulin analogs has not shown dramatic benefits on long-term outcomes.
  - The injectable rapid-acting insulin analogs are basically identical in their safety, efficacy, and kinetics.
    - Fiasp has been shown to have faster onset and peak action by 5 to 10 minutes. Its effect on HbA1c, however, has demonstrated, at best, minimal improvement to noninferiority.
  - The SORELLA trials for Admelog in T1DM and T2DM were well-designed with appropriate primary and secondary endpoints. The study populations were quite representative of the real world situation, particularly around age, duration of disease, obesity, and renal disease. Non-Caucasians were underrepresented. In the T1DM study, the authors acknowledged they did not rely on C-peptide determinations to define the group.
  - Afrezza has clearly demonstrated quicker onset and a sharp early peak effect. It appears to have less weight gain and probable decreased hypoglycemia risk. Studies have not shown consistent or clinically significant HbA1c lowering over comparator rapid insulins. It serves people who have a need for flexibility and convenience, or patients who are needle-resistant/phobic. It may have a place in patients with T2DM who have been holding back from starting insulin by offering an injection-free option.
  - Afrezza may have a little less weight gain and hypoglycemia vs the injectable rapid-acting insulins, but there are other safety concerns. Candidate selection is difficult, as it cannot be used in smokers, asthma, or COPD. It requires a rigorous and expensive lung function screening, causes cough, and may cause lung function to decline. Additionally, there is imprecision in the dosing and some information that exercise alters its kinetics. These limitations have likely kept Afrezza from becoming a game changer.
- **Disclosure of financial relationships:**
  - No potential conflicts of interest identified

APPENDIX

- **ADA guideline levels of evidence** *(ADA 2018)*

Level of Evidence	Description
A	• Clear evidence from well-conducted, generalizable RCTs that are adequately powered, including: ◦ Evidence from a well-conducted MC trial ◦ Evidence from a meta-analysis that incorporated quality ratings in the analysis • Compelling nonexperimental evidence, ie, "all or none" rule developed by the Centre for Evidence-Based Medicine at the University of Oxford • Supportive evidence from well-conducted RCTs that are adequately powered, including: ◦ Evidence from a well-conducted trial at 1 or more institutions ◦ Evidence from a meta-analysis that incorporated quality ratings in the analysis
B	• Supportive evidence from well-conducted cohort studies ◦ Evidence from a well-conducted prospective cohort study or registry ◦ Evidence from a well-conducted meta-analysis of cohort studies • Supportive evidence from a well-conducted case-control study
C	• Supportive evidence from poorly controlled or uncontrolled studies ◦ Evidence from RCTs with 1 or more major or 3 or more minor methodological flaws that could invalidate the results ◦ Evidence from observational studies with high potential for bias (such as case series with

	comparison with historical controls) ○ Evidence from case series or case reports • Conflicting evidence with the weight of evidence supporting the recommendation
E	• Expert consensus or clinical experience

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Therapeutic Class Review created by: C.Ellsworth, Pharm.D., BCPS
Reviewed by: J. D'Aloia, Pharm.D.
Publication date: 5/3/2018

OPTUMRX

SUBJECT: FORMULARY MANAGEMENT COMMITTEE CHARTER AND POLICY

POLICY ADOPTED: January 2018

POLICY REVISED: APRIL 25, 2018

SCOPE

This Policy outlines the responsibilities and activities of the Formulary Management Committee ("FMC") of OptumRx.

INTRODUCTION AND PURPOSE

FMC provides pharmacy management decisions for the OptumRx Formularies (OptumRx National Formularies, Innoviant Formulary, Legacy Catamaran Formularies and other formularies as determined by the business. FMC makes final classification on the placement of a Food and Drug Administration ("FDA") approved prescription drug to an assigned tier, exclusion programs or other clinical coverage programs and whether utilization management tools ("UM"), such as, prior authorizations, quantity limits, and step therapies, should be applied based on P&T designations and recommendations. In addition, FMC provides tier and coverage recommendation to Clients for consideration on custom formularies upon request.

COMPOSITION

FMC shall have the following voting members:
Clinical

Senior Vice President, Chief Pharmacy Officer
Vice President, Clinical Services
Senior Director, Drug Intelligence
Senior Director, Clinical Formulary Strategy
Senior Director, Utilization Management

Industry Relations

Senior Vice President,
Vice President, Industry Relations - Part D
Vice President, Industry Relations - Commercial
Vice President, Industry Relations
Senior Director, Industry Relations - Commercial
Senior Director, Industry Relations - Part D

Clinical Consulting/Client Management/Specialty Client Management
Vice President, Clinical Consulting

Vice President(s), Client Management

Vice President, Specialty Pharmacy Client Management

Senior Clinical Consultant
Senior Director, Clinical Account Management – UHC Relations
UMR Clinical Program Consultant
UMR Clinical Consultant

The following individuals shall serve on FMC as nonvoting, advisory members:
Vice President, Formulary Operations
Director, Formulary Operations
Director, Industry Relations – Commercial
Project Manager, Formulary Operations

The Director, Formulary Operations shall serve as the FMC Chairperson. The FMC Chairperson shall appoint other voting and advisory Committee members, including a Vice Chairperson and Secretary, who is capable of carrying out the responsibilities of the Committee. Committee attendance and membership is limited to employees of UnitedHealth Group (UHG). Consultants, client representatives and representatives of pharmaceutical, biologic or device manufacturers are excluded from membership and may only attend Committee meetings as invited guests, at the discretion of the FMC Chairperson, for the purpose of providing presentations or other information. In the event of the absence of a voting member, the absent voting member may designate a non-voting member to take their place during the FMC Meeting.

MEETINGS

FMC meets on a monthly basis. The FMC Chairperson may convene additional meetings as necessary to conduct FMC business. FMC members are expected to attend all meetings.

A quorum is achieved at monthly meetings when at least fifty percent (50%) of FMC's voting members from each group are present.
A motion or decision is passed or approved by an affirmative vote of at least fifty percent (50%) of the voting members present at a duly held meeting. All voting FMC members have the authority to vote on official FMC motions and decisions. Guests in attendance at FMC meetings do not have the authority to vote.

The agenda and meeting materials shall be provided to FMC members sufficiently in advance of meetings to enable FMC members to review materials in advance and participate actively in the discussion and decision-making. OptumRx staff shall maintain results of the FMC meeting in meeting minutes. OptumRx shall retain the minutes in accordance with UHG's document retention policies and procedures. The FMC meeting minutes, unless otherwise provided in relevant law or regulation, are for internal use only.

RESPONSIBILITIES OF THE CHAIRPERSON

Responsibilities of the FMC Chairperson include:

- Coordinating and conducting FMC meetings;
- Finalizing the meeting agenda and ensuring that meeting materials are provided in advance of meetings;
- Facilitating the discussion;
- Managing FMC support activities performed by OptumRx staff members;
- Ensuring appropriate documentation and distribution of FMC meeting minutes; and
- Ensuring that decisions are promptly communicated.

RESPONSIBILITIES AND DUTIES OF THE COMMITTEE

Responsibilities of FMC include, but are not limited to, the following:

- Formulary Strategy: FMC is responsible for reviewing evidence provided by the OptumRx National P&T Committee ("P&T Committee") and OptumRx staff members in recommending the assignment of FDA approved new drugs, existing drugs with new indications or new dosage forms, or drugs that otherwise have new evidence, within the OptumRx National Formulary and/or FMC's final recommendations for other Client's formularies. FMC will receive from the P&T Committee Drug Classification Designations as identified in **Exhibit A**, which may be updated from time to time based on the P&T Committee's current practices. FMC will use the Drug Classification Designations to make decisions and/or recommendations about the Formulary structure as outlined in **Exhibit B**, which may be amended from time to time to reflect FMC's current practices. In addition to the Drug Classifications Designations, FMC will also consider economic, pharmacoeconomic, and business/benefit strategy analyses (as defined below) in making Formulary placement decisions.
    - Economic evidence may include, but is not limited to, the drug's acquisition cost, including rebate information, and market and utilization data.
    - Pharmacoeconomic evidence may include, but is not limited to, the drug's impact on medical cost and quality, and cost offset.

  Once FMC has decided on the structure for the OptumRx National Formularies, such decisions shall be reviewed by the P&T Committee for clinical concerns as required by law or as required or as determined by FMC.

- Clinical Program Strategy: FMC also provides economic guidance into the type of utilization management tools ("UM") for use with particular drugs or a particular Formulary, including, but not limited to, prior authorizations, quantity limits, step therapies, and provider education. FMC makes these decisions by considering clinical, economic and pharmacoeconomic evidence (as available) provided by the P&T Committee, OptumRx staff, and other supporting financial, business and benefit strategy analyses. FMC reviews and considers recommendations and other information, including, but not limited to:

- Recommendations either from the P&T Committee or other sources regarding the use of UM tools; UM tools recommended as a result of specific drug safety concerns must be included as part of the clinical strategy program
- Prior authorizations (including step therapy and quantity limits) reviewed and approved by the P&T Committee or a subcommittee of the P&T Committee to whom the P&T Committee has delegated its authority.

COMMUNICATION

FMC will deliver all approved decisions to SVP of Clinical, and SVP of Industry Relations, for their reference.

FMC will deliver final decisions to the Benefit Implementation Committee ("BIC") for implementation and communication to internal and external stakeholders. Refer to BIC Charter. Depending on the terms of the Client's contract, the Account Management Team will either provide the FMC final recommendations or the OptumRx National Formularies to the Client. When FMCs final recommendations are provided to Clients for review and approval, the Client makes the final decision regarding the Formulary structure and management, creating a Client-specific Formulary. When the Client chooses to implement the OptumRx National Formulary as recommended as the Formulary for that particular Client's pharmacy benefit plan, FMC makes the final decision regarding the structure of the OptumRx National Formulary, which is then provided to the Client for final approval. In either circumstance, OptumRx will provide supporting documentation regarding its Formulary recommendations if such information is requested by the Client and provided for under the terms of the Client's pharmacy benefit management contract. Following receipt of Client's approval of either the recommendations or the OptumRx National Formulary, OptumRx Account Management teams shall communicate Formulary positions or utilization management assignments, reassignments or other decisions to affected staff and business groups promptly following the final decision.

The description of the Formulary management and clinical program strategy process contained in this policy is intended to be shared with our constituencies, including customers, regulators, consumers and physicians; however the underlying analytics of specific decisions are confidential, proprietary information.

CONFIDENTIALITY

During the course of participation in FMC, voting members, advisory members, and other participants ("Participants") may become aware of, develop for OptumRx, or come into possession of confidential or proprietary information. In order to protect the confidentiality of this information, Participants will adhere to the guidelines in the UHG Confidentiality Policy for Participants in Business Implementation Committee.

CONFLICT OF INTEREST

Participants must review the Conflict of Interest Policy for Participants in the Formulary Management Committee upon their appointment to FMC and annually thereafter. Participants must update their Conflict of Interest Attestation any time their circumstances change in order to ensure their information is current.

Participants must disclose any existing or potential conflicts of interest to the FMC Chairperson and Legal Counsel upon becoming aware of such conflict of interest or potential conflict of interest. Participants shall not participate in any Committee meeting until such disclosure has been made. If a Participant has questions or doubts as to whether an interest or activity is or may constitute a conflict of interest, Participant should initially consider the activity or interest to be a conflict and should provide the FMC Chairperson and Legal Counsel with the appropriate disclosure.

The decision as to whether or not a Participant may participate in any portion of a Committee meeting where a conflict may arise and in what capacity, if any, such participation is permissible, shall be made by the Committee Chairperson in consultation with Legal Counsel. In any case, a Participant may choose to recuse him/herself at any time.

Approvals of the FMC Charter and Policy:

FMC Chairperson Date

OptumRx CEO Date

Exhibit A
OptumRx Pharmacy and Therapeutics Committee Designations

P&T Committee Designations	Characteristics
Essential Drug: *Modifier:* (specify the significant unmet need fulfilled and the affected population) *Examples*: Glucophage (metformin); Entresto (sacubitril-valsartan); Zetia (ezetimibe)	A drug which has a documented clinically significant, unique therapeutic benefit in efficacy and/or safety relative to other therapeutic alternatives (where available) used to treat, manage or prevent the same or similar medical condition(s), as supported by the preponderance of available peer reviewed published data (including product labeling and information available as part of FDA review), in the overall target
Essential Class*: *Modifier:* (Define the class; explain why the class is "essential") *Clinical Note:* (Specify any niche for which a drug is essential, if any exists) *Examples*: Angiotensin converting enzyme inhibitors, Glucagon-like Peptide-1 (GLP-1) Receptor Agonists; Opioid-Induced Constipation Agents	• Drugs which, as a group, demonstrate a clinically significant, unique therapeutic benefit and have comparable safety and efficacy to one another when used to treat, manage or prevent the same or similar medical condition(s) • Drugs as a group that are similar in their pharmacology, and/or indications for use which may include individual drugs that fulfill an unmet need for a specific patient population
Unique Risk Issues: (specify the risk(s) posed) *Examples*: Ketek (telithromycin), Demerol (meperidine)	Drug(s) which, as compared to other therapeutic alternatives to treat the same or similar medical condition, have a documented increased risk of harm that substantially outweighs potential benefits, as supported by the preponderance of available peer reviewed published data (including product labeling and information available as part of FDA review) and/or based on documented action taken by a US regulatory body
Additional Data Required *Examples*:	Insufficient evidence available for the P&T Committee to weigh the clinical risks & benefits of the drug or compare it to other therapeutic options but additional data is expected within next 12 months. Drugs designated as "additional data required" shall be re-evaluated at a subsequent P&T meeting when new or additional clinical studies or evidence are available.
Optional Inclusion*: *Modifier:* (specify the reason why inclusion does not fulfill an unmet need) *Examples*: Flagyl ER (metronidazole), Addyi (flibanserin), Oralair (multiple allergens extract); Avycaz (cetazidime-avibactam)	• Drug(s) that are safe and effective, but provide no unique therapeutic benefit relative to other alternatives to treat, manage, or prevent medical condition(s) • Drug(s) that have limited evidence demonstrating safety and/or efficacy • Drug(s) that have adequate data as supported by the preponderance of available peer reviewed published literature (including product labeling and information available as part of FDA review) demonstrating the drug provides a unique therapeutic benefit for a small sub-population where the majority of clinical need could be met by other therapies

Non-Essential Non-FDA-Approved Drug *Examples*: Benziq (benzoyl peroxide 5.25% gel), Levsin (hyoscyamine); : choline magnesium trisalicylate tablets; Disalcid (salsalate) tablets	Applicable to drugs that are not approved by the FDA
Vaccine *Examples*: Menveo (meningococcal [A, C, Y, AND W-135] conjugate vaccine, Gardasil 9 ((human papillomavirus 9-valent vaccine, recombinant); Quadracel (DTaP-IPV)	Includes agents for vaccine-preventable diseases

Exhibit B

Formulary Management Committee Guidelines

P&T Committee Designations	Implications to Formulary Management Committee
Essential Drug (Specify the reason why and/or the population.)	FMC shall adhere to the following guidelines with respect to the Formulary/PDL placement of essential drugs: • Essential drugs must be available to treat the indication which rendered the drug an essential drug on an unrestricted basis, except for such restrictions that are medically indicated and appropriate. • The Formulary/PDL placement of essential drugs must comply with all legal and regulatory requirements. • The Formulary/PDL tier placement must be at least equivalent to other single source products within the same therapeutic category or products to treat the same disease state. • ORx: preferred or non-preferred tier • An uptier requires alternative in lower tier. • Cannot be Excluded • Essential drugs may not be placed on a higher copayment or coinsurance tier than the drug would otherwise be placed given the applicable scientific evidence, pharmacoeconomic factors, benefit design and other criteria used to ensure appropriate, safe and cost effective drug therapy. • The FMC shall periodically review its Formulary/PDL to ensure that the Formulary/PDL design does not discriminate or substantially discourage enrollment by certain groups. • Contracts with pharmaceutical manufacturers and other third parties must be consistent with this policy. • The FMC shall conduct reviews, but not less than once a year, to ensure that essential drugs have been placed on Formulary/PDL in accordance with these policies.
Essential Class (Specify what constitutes the class.)	• FMC will determine which of the drugs (at least one) in the particular class will be included on the Formulary/PDL, subject to the applicable benefit. • The Formulary/PDL tier placement must be at least equivalent to other single source products within the same therapeutic category or products to treat the same disease state. • An uptier of a drug with this designation to T3 requires alternative in lower tier. • May exclude with the availability of an exception process if Clinical Note specifies that access must be maintained for a specific population or indication
Unique Risk Issues: (Specify the reason why and/or the population)	FMC will take actions to limit use of Unique Risk Issues drug designations. This may include any of the following: • Placing the drug in higher Formulary/PDL tier within open formularies • Excluding the drug from closed Formularies/PDLs • Requiring Utilization Management controls designed to limit inappropriate use as recommended by the P&T Committee • Enrollee, pharmacy, and prescriber education programs

	• Online messaging to dispensing pharmacists
Additional Data Required	Drugs designated Additional Data Required will remain excluded or non-preferred within open Formularies/PDLs and will not be added to closed Formularies/PDLs. *Drugs on the New Drugs to Market (NDTM) list that are still awaiting final P&T review of Additional Data by the 6 month decision date, may stay on the NDTM list as per policy, until final P&T designation.
Optional Inclusion with Notes	• FMC will determine Formulary/PDL status of Optional Inclusion drugs. • May exclude with the availability of an exception process if Clinical Note specifies that access must be maintained for a specific population or indication • Typically T3 but rebate may allow for lower tiering. • Tier cannot be lower than Essential Drug within the same therapeutic category or products to treat the same disease state.
Optional Inclusion without notes	• FMC will determine Formulary/PDL status of Optional Inclusion drugs. • May exclude. • Tier cannot be lower than Essential Drug within the same therapeutic category or products to treat the same disease state.
Non-Essential Non-FDA-Approved Drug	• FMC will determine Formulary/PDL status of Non-Essential Non-FDA-Approved Drugs. • Tier cannot be lower than Essential Drug within the same therapeutic category or products to treat the same disease state. • May exclude
Vaccine	• FMC will determine Formulary/PDL status as necessary subject to the applicable benefit.
Vigilant Drug List	• Refer to Vigilant Drug List policy and procedure • Policy and procedures will be reviewed yearly to ensure conformance with FMC policy and procedures

Supplemental Response to No. 3:

As described in OptumRx's previous responses, OptumRx's Industry Relations group negotiates contracts and discounts with drug manufacturers, including manufacturers of insulin. Kent Rogers is Senior Vice President, Industry Relations, and is responsible for supervising the teams that conduct discount and contract negotiations with pharmaceutical manufacturers, including for insulin products. Gina Guinasso is also Senior Vice President, Industry Relations, and is responsible for formulary contracting strategy. Other Industry Relations personnel with responsibility for discount and contract negotiations with the three insulin manufacturers with whom OptumRx currently contracts include Magally Smith, Senior Manager of Pharmaceutical Contracting; Kathy Chang, Vice President, Industry Relations; Robert Earnest, Vice President, Industry Relations; Stephen Crowe, Director, Industry Relations; Jack Daly, Director, Industry Relations; Sandi Malone, Contract Manager; and Sanaz Sadeghi, Contract Manager.

Supplemental Response to Nos. 4a and 4b:

As described in OptumRx's previous responses, the design of plan formularies generally follows a multi-step process that begins with OptumRx's independent Pharmacy & Therapeutics ("P&T") Committee, which evaluates clinical evidence to assess a medication's role in therapy and overall clinical value.

Subject to the clinical designations and recommendations of the P&T Committee, OptumRx's Formulary Management Committee ("FMC") has authority to make decisions regarding the placement of prescription drugs on OptumRx's standard formularies. The FMC provides pharmacy management decisions for OptumRx's standard formularies and makes final classification decisions concerning the placement of FDA-approved drugs on an assigned formulary tier. The FMC also provides economic guidance about appropriate utilization management ("UM") tools for use with particular drugs or a particular formulary, including prior authorizations, quantity limits, step therapies, and provider education. Additionally, the FMC makes recommendations regarding formulary placement for many OptumRx clients that choose to create and follow custom formularies.

The FMC reviews and votes on recommendations to make changes to formulary placement for the OptumRx standard formularies, including assignment of new drugs, existing drugs with new indications or new dosages, or drugs that otherwise have new evidence concerning safety or efficacy. Requests for the FMC to make decisions or recommendations regarding formulary placement of drugs may be initiated by a range of different groups within OptumRx, including, most commonly, the P&T Committee and Industry Relations. Lynn Starmann, Vice President, Formulary Operations, is responsible for the Formulary Operations group, which facilitates the work of the FMC.

Subject to compliance with the clinical determinations of the P&T Committee, the FMC may also evaluate economic, pharmacoeconomic, and business/benefit considerations when making formulary placement decisions. OptumRx's primary business strategy in designing its standard formularies is to design formularies that are attractive to current and potential clients, particularly by providing clients with the lowest possible net cost of drugs.

The FMC generally meets on a monthly basis. It consists of eighteen voting members, including representatives from OptumRx Clinical Affairs, OptumRx Industry Relations, and OptumRx Client Management. The FMC also includes four non-voting advisory members, including the

FMC Chairperson. The current FMC Chairperson is Lynn Starmann. The concurrently produced FMC Charter identifies the committee's other participants.

A description of how formulary placement decisions are communicated to external and internal stakeholders is contained in the concurrently produced FMC Charter. Depending on the terms of a particular client's contract, the client is provided with either OptumRx's standard formularies or the FMC's final recommendations regarding a custom formulary. When a client chooses to implement OptumRx's standard formulary as recommended as the formulary for that particular client's pharmacy benefit plan, the FMC makes the final decision regarding the structure of OptumRx's standard formulary, which is then provided to the client for final approval. When a client chooses to implement a custom formulary, the FMC's final recommendations are provided to the client for review and approval and the client makes the final decision regarding the formulary structure and management, creating a client-specific formulary. Following receipt of the client's approval of either the recommendations or OptumRx's standard formulary, OptumRx's Account Management teams then communicate formulary positions or utilization management assignments, reassignments or other decisions to relevant internal stakeholders.

Supplemental Response to Request Nos. 1a, 1c

OptumRx negotiates with insulin manufacturers to obtain discounts on behalf of its clients and consumers. The discounts are established by the terms of rebate agreements with these manufacturers. While the specific terms are the result of negotiation, all of the insulin manufacturers pay rebates under the agreements if, and to the extent that, a particular drug receives specified formulary placement. Rebates are generally calculated as discounts off of a manufacturer's wholesale acquisition costs ("WAC"). The agreements generally define WAC to be the distributor list price for a drug as published in Medi-Span or a mutually agreed upon third party publication as of the date that the drug is dispensed.

OptumRx's rebate agreements with insulin manufacturers do not obligate OptumRx or any of its clients to provide any insulin product or other drug with any specific, preferred, or minimum placement on the OptumRx standard formularies or any custom formulary adopted by any OptumRx client. Rather, under the agreements the manufacturers make certain rebate payments if, and to the extent that, a manufacturer's drug receives a specified formulary placement. For example, an insulin manufacturer will typically pay a larger rebate for drugs that receive preferential formulary placement, which may include, for example, placement on a preferred formulary tier or absence of utilization controls unless clinically appropriate. OptumRx's rebate agreements with insulin manufacturers make clear that neither OptumRx nor its clients are obligated to grant the manufacturers preferred formulary placement for insulin products or other drugs, or to conform to the placement that creates eligibility for the agreed upon rebates. OptumRx and its clients are generally free under the rebate contracts to change their formularies at any time and without penalty.

In other words, OptumRx negotiates with insulin manufacturers regarding the conditions under which insulin purchases by its clients may become eligible to earn rebates. By lowering the net cost of insulin products, these rebates may create an incentive, but not a binding obligation, to grant preferred formulary placement to a manufacturer's product.

Commercial rebate agreements with insulin manufacturers contain administrative fees for insulin products in consideration for OptumRx's administrative services, including, but not limited to, providing general maintenance, administration, and oversight of the manufacturer's rebate program as well as negotiating and contracting with payors participating in the rebate program. The administrative fee is not charged on Qualified Prescription Drug Coverage Plans ("QRPDP"), Managed Medicaid, and CHIP utilization, and any other utilization where such fees are prohibited by law. OptumRx also does not collect any administrative fees under its Medicare rebate agreements. Administrative fees are calculated as a percentage of WAC per unit of each insulin product.

A number of OptumRx's rebate contracts with insulin manufacturers include price protection provisions, which generally provide that a manufacturer that increases its prices by more than a certain percentage over a specified period must rebate the incremental revenues above that percentage to OptumRx. Price protection provisions for insulin products are a tool to discourage insulin manufacturers from imposing significant price increases because they eliminate the manufacturers' financial incentive to do so. OptumRx passes through these payments to its clients in accordance with the clients' contracts.

OptumRx's clients retain complete and exclusive discretionary authority over their plans, and are responsible for administering, managing, and operating such plans, including establishing

and amending a plan's formulary and utilization management programs, such as prior authorization and step therapies.

Formulary Management Committee (FMC) Meeting

Tina Chuong

April 25, 2018

OPTUM Rx®

Essential Class - 2

FMC APPROVED

Recommendation: At least 1 agent within the class should be formulary; consider clinical notes

Class	Clinical Notes
[redacted]	
Long-acting insulin analogs	

[redacted]

OPTUM Rx

Formulary Ops – NDTM

FMC APPROVED

Rationale for Review

- NDTM products are set to term off list within next 60 days
- Decision needed for future management:
  1. Setup on an exclusion list (i.e. Premium Exclusion) OR
  2. Allow NDTM product to term at scheduled date and default to Select tier

Product	Therapeutic Class	Term Date (NDTM)	Future Premium Tier
[redacted]			
ADMELOG	INSULIN	7/4/2018	Exclude via PEL
ADMELOG SOLOSTAR	INSULIN	7/4/2018	Exclude via PEL
[redacted]			

Recommendation

- All products should remain on NDTM until scheduled term date, unless deemed as "Essential Drug" at P&T
- Essential drugs cannot be excluded and it will be termed from NDTM exclusion list per DI recommendations

OPTUMRx

FMC APPROVED

EHB FORMULARY CHANGES effective 1/1/2019

CLASS	DRUG	GENERIC DESC	EHB Base	EHB Enhanced
[redacted]				
Insulins	APIDRA	INSULIN GLULISINE INJ 100 UNIT/ML	T3 → EX	T4 → EX
Insulins	LEVEMIR	INSULIN DETEMIR INJ 100 UNIT/ML	T3 → T2	T4 → T3
Insulins	APIDRA SOLOSTAR	INSULIN GLULISINE SOLN PEN-INJECTOR INJ	T3 → EX	T4 → EX
Insulins	LEVEMIR FLEXTOUCH	INSULIN DETEMIR SOLN PEN-INJECTOR	T3 → T2	T4 → T3
Insulins	TRESIBA FLEXTOUCH	INSULIN DEGLUDEC SOLN PEN-INJECTOR	EX → T2	EX → T3
[redacted]				

FMC APPROVED

Formulary Ops – EHB Updates Post FMC

Rationale for Exclusion

- Exclude for EHB 1/1/2019 (Premium PEL exclusions)

Drug	Therapeutic Class	Key Points
[redacted]		
APIDRA	Insulins	PEL
APIDRA SOLOSTAR	Insulins	PEL
[redacted]		

+ Me Too
* High Cost Generic
^ NEDEL
PEL = Premium Exclusion List

OPTUM Rx

Formulary Management Committee (FMC) Meeting

Tina Chuong

May 30, 2018

OPTUM Rx®

Essential Class

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Recommendation: At least 1 agent within the class should be formulary; consider clinical notes

[redacted]	
Rapid-acting insulins	
[redacted]	

[redacted]

OPTUM Rx

NDTM

FMC APPROVED

[redacted]				
ADMELOG and ADMELOG SOLO (INSULIN LISPRO)	INSULIN	Essential Class	NDTM (term 7/4/2018)	No change
[redacted]				

OPTUM Rx

Formulary Management Committee (FMC) Meeting

Tina Chuong

June 27, 2018

OPTUM Rx®

Therapeutic Categories for Review - 2019

[redacted]

4) Diabetes (Basal Insulins) [redacted]

[redacted]

2019 Summary of Changes - 1

Therapeutic Class	Drug Name	Premium		Select	
		Current	Proposed	Current	Proposed
[redacted]					
Basal Insulin	Tresiba	Excluded	Excluded	T3	T2
[redacted]					

FMC approved pending P&T approval

Diabetes (Basal Insulins) – Tresiba

RATIONALE FOR REVIEW

- Tresiba is a basal insulin product that was approved by the FDA in Dec 2016. The basal insulin class was evaluated as part of 2019 recontracting effort to leverage competition and reduce the overall cost of the category.
- Tresiba is a long-acting, once-daily basal insulin analog indicated for patients 1 year of age or older with type 1 and or type 2 diabetes. It is available as a 100-unit/ml and 200-unit/ml prefilled pen

KEY POINTS

- **P&T Designation:** Essential Class
- A1C reduction and CV safety for Tresiba is similar to insulin glargine. Tresiba has less hypoglycemic episodes and nocturnal hypoglycemic episodes compared to insulin glargine
- Tresiba can be administered at any time during the day, allows for flexibility in dosing administration.
- Tresiba continues to gain market share despite Non-Preferred Brand status on Select Formulary
- Adding Tresiba to T2 will provide another alternative to patients in a class that is continuing to grow.
- Annual rebate impact: Redacted

RECOMMENDATION

	Current Tier / UM	Proposed Tier / UM
Premium Formulary	Excluded	Excluded
Select Formulary	Tier 3	Tier 2 [eff 1/1/19]

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Diabetes (Basal Insulins) – Drug Level Data

DRUG LEVEL DATA (4Q17)							TIER COMPARISON		
MFG	Drug	Dosage Form	Rx / Qtr	Pts / Qtr	IC / Rx	Net Cost/Rx	ORx Select	ORx Prem	UHC E&I
Lilly	Basaglar	SOPN	5,424	3,266	Redacted	Redacted	3^	EXCL	1*
Novo	Levemir	SOPN/SOL N	22,566	13,600	Redacted	Redacted	2	EXCL	2*
Sanofi	Lantus	SOPN/SOL N	114,494	70,485	Redacted	Redacted	2	2	EXCL
Sanofi	Toujeo	SOPN	28,209	16,106	Redacted	Redacted	2	2	EXCL
Novo	**Tresiba**	**SOPN**	**13,268**	**8,145**	Redacted	Redacted	**3**	**EXCL**	**NF***

† Subject to prior authorization * Subject to quantity limits ^ Step Therapy

- **Member Impact**
  - Positive impact – Tresiba downtier for Select Formulary. Member cost share reduction for an additional basal insulin product

OPTUM Rx

[redacted]

Essential Class - 3

Recommendation: At least 1 agent within the class should be formulary; consider clinical notes

Class	Clinical Notes
Rapid-acting insulins	

[redacted]

FMC approved

Formulary Ops – NDTM

Rationale for Review

- NDTM products are set to term off list within next 60 days
- Decision needed for future management:
  1. Setup on an exclusion list (i.e. Premium Exclusion) OR
  2. Allow NDTM product to term at scheduled date and default to Select tier

Product	Therapeutic Class	Term Date (NDTM)	Future Premium Tier
[redacted]			
ADMELOG (new NDC)	Insulin	7/4/2018	EXCLUDED

Recommendation

- All products should remain on NDTM until scheduled term date, unless deemed as "Essential Drug" at P&T
- Essential drugs cannot be excluded and it will be termed from NDTM exclusion list per DI recommendations

OPTUM Rx

Formulary Management Committee (FMC) Meeting

Trang Tran

August 29, 2018

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FMC Approved

Diabetes

Rationale for Review:

- 2019 Contract Changes
- Revise current ST requirements: Add Tresiba to list of step 1 alternatives.
- Effective 1/1/19

Current UM:

Therapeutic Category	Current UM: ST	Recommended Changes
Basal Insulin	Preferred Agents: Lantus, Levemir, Toujeo Non-preferred Agents: Basaglar	Preferred Agents: Lantus, Levemir, Toujeo, Tresiba Non-preferred Agents: Basaglar

Formulary Management Committee (FMC) Meeting

Tina Chuong

January 23, 2019

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FMC Approved

Essential Class - 3

Recommendation: At least 1 agent within the class should be formulary; consider clinical notes

Class	Clinical Notes
Long-acting insulin analogs	

[redacted]

Note: Refer to the P&T Decision Grid for all of the agents within each class. Refer to the Agenda Summary/FMC Grid for the clinical notes.


Formulary
Management
Committee
(FMC) Meeting
Tina Chuong
May 29, 2019
OPTUM Rx

Approved Ad-hoc FMC Proposals

[redacted]

- Humalog (insulin lispro)

Humalog (insulin lispro) – Summary

RATIONALE FOR REVIEW

- Humalog ABA products are expected to launch in early May 2019
- Reevaluation of the Humalog brand and ABA products needed to address market dynamics
  - Additional rebate opportunities available for the various benefit designs

FINANCIAL EVALUATION

- For OptumRx Commercial LOB, Humalog PMPM = Redacted
- Premium: net costs of Humalog brands are lower than the ABAs
- Select Comprehensive: net costs of Humalog brands and ABAs are comparable
- All other plan types: net costs of Humalog ABAs are lower than brands

KEY POINTS

- For Premium, recommend to continue the exclusion of Humalog ABA products as the brands are the lowest net cost products
- For Select, recommend to downtier Humalog ABA products to T2 with ST, which will help drive to lower cost products
- The strategy is to balance client agreements while passing the savings to clients and members

FMC Approved via email vote

Humalog (insulin lispro) – Financial Analysis

Drug	Tier/UM					PRICING DATA	
Drug Name	Select		Premium		Eff Date	WAC/ Rx	Net WAC/ Rx
	Current	New	Current	New			
Humalog vial	2	2	2	2	n/a	$288.44	Redacted
Humalog Kwikpen	2	2	2	2	n/a	$404.52	Redacted
Insulin Lispro vial (ABA)	3^	2^	EXCL	EXCL	5/2/2019	$144.27	Redacted
Insulin Lispro Kwikpen (ABA)	3^	2^	EXCL	EXCL	5/2/2019	$202.26	Redacted

^ Step Therapy (step through both Humalog and Novolog brand products pending P&T approval)

Premium: Remove from NDTM early and add to PEL effective 5/2/19

OPTUMRx®

**FIFTH (5TH) AMENDMENT TO THE
OPTUMRX, INC.
REBATE AGREEMENT**

This FIFTH (5th) AMENDMENT TO THE OPTUMRX, INC. REBATE AGREEMENT ("Amendment"), dated as of July 1, 2015 ("Amendment Effective Date"), is made and entered into by and between, sanofi-aventis U.S. LLC, on behalf of itself and its affiliate Genzyme Corporation, ("Manufacturer"), and OptumRx, Inc. ("Administrator"), on behalf of itself and its Contracting Payors, with reference to the following facts:

RECITALS

WHEREAS, Manufacturer and Administrator entered into that certain Rebate Agreement (as previously amended, the "Agreement"), with an effective date of January 1, 2013, providing, among other things, for Manufacturer to pay rebates to Administrator on units of certain Manufacturer Drugs; and

WHEREAS, Manufacturer and Administrator mutually desire to amend the Agreement as stated below.

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Manufacturer and Administrator hereby agree to amend the Agreement as follows:

1. Exhibit A Rebate and Administrative Fee Schedule of the Agreement is hereby deleted its entirety and replaced with the following new Exhibit A Rebate and Administrative Fee Schedule attached hereto.

2. Exhibit D of the Agreement is hereby deleted in its entirety and replaced with the following new Exhibit D attached hereto.

3. Effect of this Amendment. Capitalized terms used but not defined in this Amendment shall have the meanings ascribed to them in the Agreement. Except as otherwise amended by this Amendment, all other terms and conditions of the Agreement shall remain in full force and effect. In the event there is any inconsistency or conflict between the provisions in this Amendment and those in the Agreement, the provisions in this Amendment shall supersede and control.

SIGNATURE PAGE FOLLOWS

IN WITNESS WHEREOF, Manufacturer and Administrator have executed this Amendment as of the date first written above.

ADMINISTRATOR

By: Robert C. Lahman

Name: Robert C. Lahman

Title: S.V.P., Industry Relations

Date: 12-4-2015

MANUFACTURER

By: James Borneman

Name: James Borneman

Title: Vice President Strategic Pricing & Contracting

Date: 12/8/15

MANUFACTURER

By: Gregory Rubert

Name: Gregory Rubert

Title: Sr. Director Managment Reporting

Date: 12/8/15

EXHIBIT A
REBATE AND ADMINISTRATIVE FEE SCHEDULE

1. Definitions

1.1 Benefit Design

i. "Covered" means a Benefit design that does not qualify as a Managed or Highly Managed Benefit design.

ii. "Managed" means a Benefit design characterized by a Formulary under which the Contracting Payor directly or indirectly influences availability or gives preference in dispensing decisions of Drugs in the same Defined Drug Market through monetary restrictions; for example, differential dollar Consumer co-payments for generic, branded Preferred and branded non-Preferred status as defined and determined by the Contracting Payor, where branded non-Preferred Drugs and branded Preferred Drugs have no less than an average co-payment differential of ten dollars ($10.00), or an equivalent co-insurance percentage differential.

iii. "Highly Managed" means a Benefit design characterized by a Formulary under which a Contracting Payor also has the ability, and in fact exercises such ability, to directly or indirectly influence availability or give preference in dispensing decisions of Drugs in the same Defined Drug Market through hard edit prior authorizations, NDC locks for non-Preferred Drugs, step edits, or other similar mechanisms where certain Drugs are intended to be more restricted in availability than other Preferred Drugs in the same Defined Drug Market.

1.2 "Formulary Status" means the position a Manufacturer Drug has on Formulary. A Formulary Status that is designated as 1 of [X] means that the Manufacturer Drug is 1 of [X] single-source branded Drugs in the Defined Drug Market with the applicable Formulary Status; provided that for the purpose of determining if this condition for Rebate has been met, line extensions of Drugs within the Manufacturer Drug's Defined Drug Market manufactured by the same manufacturer shall be considered as one Drug (e.g. [redacted]

1.3 "Preferred" means (i) a Drug is covered by a Benefit and is adjudicated in the lowest copayment tier for branded Drugs for the applicable Defined Drug Market and where the copayment amount or coinsurance percentage for such Drug is lower than that of Drugs in the Defined Drug Market designated as "non-preferred", or (ii) a Drug is covered by a Benefit where the Drugs designated as "preferred" are covered by the Benefit and the Drugs excluded from Formulary or designated on Formulary as "non-preferred" or "excluded" are not covered by the Benefit or (iii) for Covered Benefit designs only, a Drug is covered by a Benefit where Drugs designated as "preferred" are covered by the Benefit and Manufacturer Drug is no more restricted in its availability than other branded Drugs in the same Defined Drug Market.

1.4 "Unrestricted Access" when referring to Lantus means a Manufacturer Drug is covered by a Benefit with no Utilization Controls. But when referring to all other Manufacturer Drugs, means a Manufacturer Drug covered by a Benefit with no Utilization Controls, except for the allowances set forth in 1.5 Utilization Controls.

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1.5 "Utilization Controls" mean, unless such Utilization Controls applied are clinically appropriate in accordance with FDA labeling or indications and/or applied to all Drugs in the applicable Defined Drug Market, i) counter-detailing or counter-promoting, ii) switching or therapeutic substitution, iii) hard edit prior authorization, iv) NDC lock, v) step edit, and vi) quantity limit based upon package insert. For purposes of this definition, "Utilization Controls" excludes communications or education programs designed to encourage the use of generic Drugs, and any aspects of Administrator's or Contracting Payor's communication, website, or other activity whereby Consumers have access to or are made aware of prices of Drugs and/or the availability of over-the-counter products for purposes of managing Consumer cost sharing amounts.

2. Rebate Calculation

Rebates for each Manufacturer Drug will be based upon the Formulary status of the Manufacturer Drug at the time such Manufacturer Drug is dispensed. Rebates will be calculated on a per Unit dispensed basis. For each month, the Rebates for each Manufacturer Drug shall be calculated as follows:

Rebate = (Unit(s) of Manufacturer Drug) x (WAC) x (Total Rebate Rate for the applicable Manufacturer Drug)

3. Administrative Fee. The Administrative Fee rate is 3% for each Rebate eligible Unit of Manufacturer Drug. The Administrative Fee shall not be charged on QRPDP, Managed Medicaid and CHIP utilization, and any other utilization where prohibited by Law. For each month, the Administrative Fee shall be calculated as follows:

Administrative Fee = (Unit(s) of Manufacturer Drug) x (WAC) x (Administrative Fee rate %)

4. Protection of Rebate Amount.

4.1 [redacted] and Lantus Price Protection

Rebate rates are subject to automatic adjustment in the event the "WAC per Unit" for Manufacturer Drug is increased to a price that is greater than the "Allowed WAC per Unit" during any corresponding month of the Agreement. The initial "Allowed WAC per Unit" for a Manufacturer Drug is calculated by multiplying the "WAC per Unit" as of the date set forth in the Rebate terms below ("Baseline WAC Date") for the applicable Manufacturer Drug by (100% plus the "Price Protection" factor). The "Net WAC per Unit" is calculated by multiplying the "WAC per Unit" by (100% minus the Base Rebate Rate %). The "Base Rebate Rate %" is the Rebate percentage for the Manufacturer Drug set forth in the applicable Rebate tables below. The "Allowed WAC per Unit" for subsequent Contract Years is calculated by multiplying the "Allowed WAC" for the previous Contract Year by (100% plus the "Price Protection" factor). The initial Allowed

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WAC per Unit for a Manufacturer Drug will apply during the 12-month period following the Manufacturer Drug's Contract Year Start Date (which date is set forth in the Rebate terms below). Such initial 12-month period and each subsequent 12- month period is referred to as the applicable Manufacturer Drug's "Contract Year". The "Net Allowed WAC per Unit" is calculated by multiplying the "Allowed WAC per Unit" by (100% minus the Base Rebate Rate %). The "Price Protection" factor is set forth in the Rebate terms below for the applicable Manufacturer Drug. Effective as of the date the "WAC per Unit" first exceeds the "Allowed WAC per Unit" and continuing for the remainder of that Contract Year, subject to further adjustments in accordance with this Section 4.1 of this Exhibit A Rebate and Administrative Fee Schedule, an "Additional Rebate Rate" will be provided. The "Additional Rebate Rate" is calculated by determining the amount, if any, that the Current Net WAC Per Unit for a given month exceeds the Net Allowed WAC per Unit for the same month, divided by the then-current WAC per Unit. The resulting percentage is the "Additional Rebate Rate" and is added to the "Base Rebate Rate %" to produce a "Total Rebate Rate" that applies during that month. The Additional Rebate Rate will be paid each month in which the "Current Net WAC per Unit" exceeds the "Net Allowed WAC per Unit". The Additional Rebate Rate is re-calculated each month. For avoidance of doubt, the Total Rebate Rate calculation for [redacted] is subject to the terms of Section 2.2.6 Best Price. [redacted]

*The terms "Current Net WAC" and "Net Allowed WAC" are solely used for purposes to explain the calculation of price protection in this Agreement. These terms are not used outside of this Agreement and, furthermore, are not meant to define or describe any pricing terms of a Manufacturer Drug.

[redacted] AND LANTUS EXAMPLE 1:

Price Protection factor	6%			Year 1 Price increase 10%						Year 2 Price increase 10%						Year 3 Price increase 10%		
	Assumed WAC as of 12/31/2013	Jan. 2014	Feb. 2014	Mar. 15 2014		Dec. 2014		Jan. 2015	Feb. 2015	Mar. 2015		Dec. 2015		Jan. 2016	Feb. 2016	Mar. 2016		Dec. 2016
Current WAC/ Unit (Existing NDC)	6.00	6.00	6.00	6.60	→	6.60		6.60	6.60	7.26	→	7.26		7.26	7.26	7.99	→	7.99
Allowed WAC/ Unit (Existing NDC)		6.36	6.36	6.36		6.36	→	6.74	6.74	6.74		6.74	→	7.15	7.15	7.15		7.15
Current WAC/ Unit (New NDC)									6.60	7.26	→	7.26		7.26	7.26	7.99	→	7.99
Allowed WAC/ Unit (New NDC)									6.74	6.74		6.74	→	7.15	7.15	7.15		7.15
Current Net WAC / Unit		5.40	5.40	5.94		5.94		5.94	5.94	6.53		6.53		6.53	6.53	7.19		7.19
Net Allowed WAC / Unit	5.40	5.72	5.72	5.72		5.72		6.07	6.07	6.07		6.07		6.43	6.43	6.43		6.43
Additional Rebate :		$0.00	$0.00	$0.22		$0.22		$0.00	$0.00	$0.47		$0.47		$0.10	$0.10	$0.76		$0.76
Additional Rebate Rate.		0.0%	0.0%	3.3%		3.3%		0.0%	0.0%	6.4%		6.4%		1.4%	1.4%	9.5%		9.5%
Base Rebate Rate %	10.0%	10.0%	10.0%	10.0%		10.0%		10.0%	10.0%	10.0%		10.0%		10.0%	10.0%	10.0%		10.0%
Total Rebate Rate	10.0%	10.0%	10.0%	13.3%	→	13.3%		10.0%	10.0%	16.4%	→	16.4%		11.4%	11.4%	19.5%	→	19.5%

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If a new NDC ("New NDC") matching the labeler code and product code ("9-digit National Drug Code" or "NDC-9") of a Manufacturer Drug covered by this Agreement comes into existence after the date that such Manufacturer Drug becomes covered by this Agreement, the Additional Rebate Rate for such New NDC(s) will be calculated consistent with the preceding paragraph except that (i) the Net Allowed WAC per Unit for the Existing NDCs (defined below) will apply to the New NDC(s) during each billing period and (ii) the Net WAC per Unit of such New NDC(s) will be adjusted to account for differences, if any, in days of therapy, unit size, strength, or similar factors, between the New NDC(s) and their corresponding Existing NDCs, which adjustment(s) the parties will work in good faith to establish. As used herein, the term "Existing NDCs" refers to the Manufacturer Drug NDC(s) covered by the Agreement on the day prior to the date that the applicable New NDC comes into existence that has the highest Net Allowed WAC per Unit; provided, however, that either party may elect for the Existing NDC to be the NDC that most closely resembles the New NDC with respect to days of therapy, unit size, strength, or similar factors, which the parties will mutually determine working together in good faith. Example 2 below demonstrates the Additional Rebate Rate calculation for a New NDC.

[redacted] AND LANTUS EXAMPLE 2:

New NDC introduced Feb14, subject to same PP rate increase as current NDCs.
New NDC WAC normalized to Current NDC WAC, same Baseline WAC date
Price Protection factor 6%

	Assumed WAC as of 12/31/2012	Jan 2013	Feb. 2013	Mar. 15 2013 (Year 1 Price increase 10%)		Dec. 2013	
Current WAC/ Unit (Current NDC)	6.00	6.00	6.00	6.60	→	6.60	
Allowed WAC/ Unit (Current NDC)		6.36	6.36	6.36		6.36	→
Current WAC/ Unit (New NDC)							
Current Normalized WAC/ Unit (New NDC)							
Allowed WAC/ Unit (New NDC)							
Current Net WAC / Unit (Current NDC)		5.40	5.40	5.94		5.94	
Net Allowed WAC / Unit (Current NDC)	5.40	5.72	5.72	5.72		5.72	
Current Net WAC / Unit (New NDC)							
Net Allowed WAC / Unit (New NDC)							
Additional Rebate (Current NDC) :		$0.00	$0.00	$0.22		$0.22	
Additional Rebate Rate (Current NDC)		0.0%	0.0%	3.3%		3.3%	
Additional Rebate (New NDC)							
Additional Rebate Rate (New NDC)							
Base Rebate Rate %	10.0%	10.0%	10.0%	10.0%		10.0%	
Total Rebate Rate (Current NDC)	10.0%	10.0%	10.0%	13.3%	→	13.3%	
Total Rebate Rate (New NDC)					→		

	Jan. 2014	Feb. 2014	Mar 2014 (Year 2 Price increase 10%)		Dec. 2014		Jan. 2015	Feb. 2015	Mar. 2015 (Year 3 Price increase 10%)		Dec. 2015
Current WAC/ Unit (Current NDC)	6.60	6.60	7.26	→	7.26		7.26	7.26	7.99	→	7.99
Allowed WAC/ Unit (Current NDC)	6.74	6.74	6.74		6.74	→	7.15	7.15	7.15		7.15
Current WAC/ Unit (New NDC)		10.50	11.55	→	11.55		11.55	11.55	12.71	→	12.71
Current Normalized WAC/ Unit (New NDC)		9.90	10.89	→	10.89		10.89	10.89	11.98	→	11.98
Allowed WAC/ Unit (New NDC)		10.11	10.11		10.11	→	10.72	10.72	10.72		10.72
Current Net WAC / Unit (Current NDC)	5.94	5.94	6.53		6.53		6.53	6.53	7.19		7.19
Net Allowed WAC / Unit (Current NDC)	6.07	6.07	6.07		6.07		6.43	6.43	6.43		6.43
Current Net WAC / Unit (New NDC)		9.45	10.40		10.40		10.40	10.40	11.43		11.43
Net Allowed WAC / Unit (New NDC)		9.10	9.10		9.10		9.65	9.65	9.65		9.65
Additional Rebate (Current NDC) :	$0.00	$0.00	$0.47		$0.47		$0.10	$0.10	$0.76		$0.76
Additional Rebate Rate (Current NDC)	0.0%	0.0%	6.4%		6.4%		1.4%	1.4%	9.5%		9.5%
Additional Rebate (New NDC)		$0.35	$1.29		$1.29		$0.75	$0.75	$1.79		$1.79
Additional Rebate Rate (New NDC)		3.3%	11.2%		11.2%		6.5%	6.5%	14.1%		14.1%
Base Rebate Rate %	10.0%	10.0%	10.0%		10.0%		10.0%	10.0%	10.0%		10.0%
Total Rebate Rate (Current NDC)	10.0%	10.0%	16.4%	→	16.4%		11.4%	11.4%	19.5%	→	19.5%
Total Rebate Rate (New NDC)		13.3%	21.2%	→	21.2%		16.5%	16.5%	24.1%	→	24.1%

	Current WAC	DOT (can be changed to whatever the 'normalization' factor should be)	Normalized WAC / per DOT	WAC in effect for New NDC
Current NDC	6.60	60	0.11	
New NDC	10.50	90		9.90

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4.2 [redacted], Toujeo and [redacted] Price Protection

Rebate rates are subject to automatic adjustment in the event the "WAC per Unit" for Manufacturer Drug is increased to a price that is greater than the "Allowed WAC per Unit" during any corresponding month of the Agreement. The "Allowed WAC per Unit" for 2013 is calculated by multiplying the "WAC per Unit" as of the date set forth in the Rebate terms below ("Baseline WAC Date") for the applicable Manufacturer Drug by (100% plus the "Price Protection" factor). The "Net WAC per Unit" is calculated by multiplying the "WAC per Unit" by (100% minus the Base Rebate Rate %). The "Base Rebate Rate %" is the Rebate percentage for the Manufacturer Drug set forth in the Rebate tables below. The initial Allowed WAC per Unit for a Manufacturer Drug will apply during the 12-month period following the Agreement's Effective Date. Such initial 12-month period and each subsequent 12-month period is referred to as the applicable Manufacturer Drug's "Contract Year". The "Allowed WAC per Unit" for subsequent Contract Years is calculated by multiplying the "WAC per Unit" in effect for the applicable Manufacturer Drug on December 31 of the Contract Year immediately prior to the current Contract Year by (100% plus the "Price Protection" factor). The "Net Allowed WAC per Unit" is calculated by multiplying the "Allowed WAC per Unit" by (100% minus the Base Rebate Rate %). For avoidance of doubt: (a) the first pricing period shall be Contract Year 2013; (b) the second pricing period shall be Contract Year 2014; (c) the third pricing period shall be Contract Year 2015; (d) the fourth pricing period shall be Contract Year 2016; and (e) the fifth pricing period shall be Contract Year 2017. Price increases in one pricing period shall not be added to price increases in another pricing period for purposes of determining Additional Rebate Rates. The "Price Protection" factor is set forth in the Rebate terms below for the applicable Manufacturer Drug. Effective as of the date the "WAC per Unit" first exceeds the "Allowed WAC per Unit" and continuing for the remainder of that Contract Year, subject to further adjustments in accordance with this Section 4.2 of this Exhibit A Rebate and Administrative Fee Schedule, an "Additional Rebate Rate" will be provided. The "Additional Rebate Rate" is calculated by determining the amount, if any, that the Net WAC Per Unit for a given month exceeds the Net Allowed WAC per Unit for the same month, divided by the then-current WAC per Unit. The resulting percentage is the "Additional Rebate Rate" and is added to the "Base Rebate Rate %" to produce a "Total Rebate Rate" that applies during that month. The Additional Rebate Rate will be paid each month in which the "Current Net WAC Per Unit" exceeds the "Net Allowed WAC per Unit". The Additional Rebate Rate is re-calculated each month. For avoidance of doubt, the Total Rebate Rate calculation is subject to the terms of Section 2.2.6 Best Price. [redacted]

*The terms "Current Net WAC" and "Net Allowed WAC" are solely used for purposes to explain the calculation of price protection in this Agreement. These terms are not used outside of this Agreement and, furthermore, are not meant to define or describe any pricing terms of a Manufacturer Drug.

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[redacted], TOUJEO, AND [redacted] EXAMPLE 1:

Price Protection factor:	6%			Year 1 Price increase 10%				Year 2 Price increase 10%			
	Assumed WAC as of 12/31/2012	Jan. 2013	Feb. 2013	Mar. 15 2013	Dec. 2013	Jan. 2014	Feb. 2014	Mar. 2014	Dec. 2014	Jan. 2015	Feb. 2015
Current WAC/ Unit (Existing NDC)	6.00	6.00	6.00	6.60	6.60	6.60	6.60	7.26	7.26	7.26	7.26
Allowed WAC/ Unit (Existing NDC)		6.36	6.36	6.36	6.36	7.00	7.00	7.00	7.00	7.70	7.70
Current WAC/ Unit (New NDC)							6.60	7.26	7.26	7.26	7.26
Allowed WAC/ Unit (New NDC)							7.00	7.00	7.00	7.70	7.70
Current Net WAC / Unit		5.40	5.40	5.94	5.94	5.94	5.94	6.53	6.53	6.53	6.53
Net Allowed WAC / Unit	5.40	5.72	5.72	5.72	5.72	6.30	6.30	6.30	6.30	6.93	6.93
Additional Rebate :		$0.00	$0.00	$0.22	$0.22	$0.00	$0.00	$0.24	$0.24	$0.00	$0.00
Additional Rebate Rate:		0.0%	0.0%	3.3%	3.3%	0.0%	0.0%	3.3%	3.3%	0.0%	0.0%
Base Rebate Rate %:	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%
Total Rebate Rate	10.0%	10.0%	10.0%	13.3%	13.3%	10.0%	10.0%	13.3%	13.3%	10.0%	10.0%

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If a new NDC ("New NDC") matching the labeler code and product code ("9-digit National Drug Code" or "NDC-9") of a Manufacturer Drug covered by this Agreement comes into existence after the date that such Manufacturer Drug becomes covered by this Agreement, the Additional Rebate Rate for such New NDC(s) will be calculated consistent with the preceding paragraph except that (i) the Net Allowed WAC per Unit for the Existing NDCs (defined below) will apply to the New NDC(s) during each billing period and (ii) the Net WAC per Unit of such New NDC(s) will be adjusted to account for differences, if any, in days of therapy, unit size, strength, or similar factors, between the New NDC(s) and their corresponding Existing NDCs, which adjustment(s) the parties will work in good faith to establish. As used herein, the term "Existing NDCs" refers to the Manufacturer Drug NDC(s) covered by the Agreement on the day prior to the date that the applicable New NDC comes into existence that has the highest Net Allowed WAC per Unit; provided, however, that either party may elect for the Existing NDC to be the NDC that most closely resembles the New NDC with respect to days of therapy, unit size, strength, or similar factors, which the parties will mutually determine working together in good faith. Example 2 below demonstrates the Additional Rebate Rate calculation for a New NDC.

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[redacted] TOUJEO, AND [redacted] EXAMPLE 2:

New NDC introduced Feb14, subject to same PP rate increase as Existing NDCs.
Same WAC/unit, same Baseline WAC date.
Price Protection factor: 6%

Year 1 Price increase 10% (Mar. 15 2013) — Allowed was 6.74 (Jan. 2014) — Year 2 Price increase 10% (Mar. 2014)

	Assumed WAC as of 12/31/2012	Jan. 2013	Feb. 2013	Mar. 15 2013		Dec. 2013	Jan. 2014	Feb. 2014	Mar. 2014		Dec. 2014	Jan. 2015	Feb. 2015
Current WAC/ Unit (Existing NDC)	6.00	6.00	6.00	6.60	→	6.60	6.60	6.60	7.26	→	7.26	7.26	7.26
Allowed WAC/ Unit (Existing NDC)		6.36	6.36	6.36		6.36	7.00	7.00	7.00		7.00	7.70	7.70
Current WAC/ Unit (New NDC)								10.50	11.55	→	11.55	11.55	11.55
Current Normalized WAC/ Unit (New NDC)								9.90	10.89		10.89	10.89	10.89
Allowed WAC/ Unit (New NDC)								10.49	10.49		10.49	12.24	12.24
Current Net WAC / Unit (Existing NDC)		5.40	5.40	5.94		5.94	5.94	5.94	6.53		6.53	6.53	6.53
Net Allowed WAC / Unit (Existing NDC)	5.40	5.72	5.72	5.72		5.72	6.30	6.30	6.30		6.30	6.93	6.93
Current Net WAC / Unit (New NDC)								9.45	10.40		10.40	10.40	10.40
Net Allowed WAC / Unit (New NDC)								9.44	9.44		9.44	11.02	11.02
Additional Rebate (Existing NDC):		$0.00	$0.00	$0.22		$0.22	$0.00	$0.00	$0.24		$0.24	$0.00	$0.00
Additional Rebate Rate (Existing NDC):		0.0%	0.0%	3.3%		3.3%	0.0%	0.0%	3.3%		3.3%	0.0%	0.0%
Additional Rebate (New NDC):								$0.01	$0.95		$0.95	$0.00	$0.00
Additional Rebate Rate (New NDC):								0.1%	8.2%		8.2%	0.0%	0.0%
Base Rebate Rate %:	10.0%	10.0%	10.0%	10.0%		10.0%	10.0%	10.0%	10.0%		10.0%	10.0%	10.0%
Total Rebate Rate (Existing NDC)	10.0%	10.0%	10.0%	13.3%	→	13.3%	10.0%	10.0%	13.3%	→	13.3%	10.0%	10.0%
Total Rebate Rate (New NDC)								10.1%	18.2%	→	18.2%	10.0%	10.0%

	Current WAC	DOT (can be changed to whatever the 'normalization' factor should be)	Normalized WAC / per DOT	WAC in effect for New NDC
Existing NDC	6.60	60	0.11	
New NDC	10.50	90		9.90

5. Rebate Terms – non-QRPDP, non-Managed Medicaid and non-CHIP

5.1 PREFERRED

Option A: (Effective 7/1/2015 through 6/30/2017)

Manufacturer Drug Name: Lantus*			
Benefit Design:	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	42%*	n/a	n/a
Administrative Fee	3%	n/a	n/a
Price Protection factor	7%	n/a	n/a
Baseline WAC Date:	1/1/14	n/a	n/a
Contract Year Start Date	7/1/14	n/a	n/a

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price.

Conditions to Rebate:

1. All NDC's of Manufacturer Drug are on Formulary with Unrestricted Access in tier 1, 2 or 3 as of the date of dispensing. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Lantus' Defined Drug Market are subject to quantity limit consistent with their respective package inserts; and
2. A certain package form of Lantus may be disadvantaged to one (1) comparable package form of another Drug in Lantus' Defined Drug Market, provided all Lantus package forms are still listed and adjudicated with Unrestricted Access in accordance with Condition 1 above. In the event that a package form of Lantus is disadvantaged to more than one (1) comparable package form, all NDC's of Lantus, i.e. both vial and pen, shall be ineligible for Rebates as of such date of dispensing. The following examples are provided for clarification of rebate eligibility and not to be considered an exhaustive list:

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Would Pay Vial and Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	3	Non-preferred	3	Non-preferred
Levemir	Vial	1	Preferred	1	Preferred
Comp #3	Vial	3	Non-preferred	3	Non-preferred
Lantus	Pen	3	Non-preferred	3	Non-preferred
Levemir	Pen	1	Preferred	3	Non-preferred
Comp #3	Pen	3	Non-preferred	2	Preferred

Would **NOT** Pay Vial or Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	3	Non-preferred	3	Non-preferred
Levemir	Vial	1	Preferred	1	Preferred
Comp #3	Vial	2	Preferred	3	Non-preferred
Lantus	Pen	3	Non-preferred	3	Non-preferred
Levemir	Pen	1	Preferred	1	Preferred
Comp #3	Pen	2	Preferred	2	Preferred

Option B: (Effective /1/2015 through 6/30/2017)

Manufacturer Drug Name: Lantus*				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 2	n/a	12%*	7%*
Administrative Fee		n/a	3%	3%
Price Protection factor		n/a	7%	7%
Baseline WAC Date:		n/a	1/1/14	1/1/14
Contract Year Start Date		n/a	7/1/14	7/1/14

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price.

Conditions to Rebate:

1. All NDC's of Manufacturer Drug are on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing; and
2. Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Lantus' Defined Drug Market are subject to quantity limit consistent with their respective package inserts; and
3. No package form of Lantus will be disadvantaged to a comparable package form of any other Drug in Lantus' Defined Drug Market. In the event that a package form of Lantus is disadvantaged to a comparable package form, all NDC's of Lantus, i.e. both vial and pen, shall be ineligible for Rebates as of such date of dispensing. The following examples

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are provided for clarification of Rebate eligibility and not to be considered an exhaustive list:

Would Pay Vial and Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	1	Preferred	1	Preferred
Levemir	Vial	1	Preferred	1	Preferred
Lantus	Pen	1	Preferred	2	Preferred
Levemir	Pen	1	Preferred	2	Preferred

Would NOT Pay Vial or Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	1	Preferred	2	Preferred
Levemir	Vial	1	Preferred	1	Preferred
Lantus	Pen	3	Non-preferred	2	Preferred
Levemir	Pen	3	Non-preferred	2	Preferred

5.2 PREFERRED

5.2(a) (Effective 7/1/2015 through 6/30/2017)

Manufacturer Drug Name: Apidra				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 2 or less	47%	47%	47%
Base Rebate Rate %	1 of 3	42%	42%	42%
Administrative Fee		3%	3%	3%
Price Protection factor		n/a	n/a	n/a
Baseline WAC Date:		n/a	n/a	n/a

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5.3 PREFERRED – EXCLUSION

5.3.1 Only for Benefit Contracts with less than two (2) million Consumers

5.3.1 (a) (Effective 7/1/2015 through 12/31/2015)

Manufacturer Drug Name: Lantus*				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 1	43%*	N/A	N/A
Administrative Fee		3%	N/A	N/A
Price Protection factor		7%	N/A	N/A

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Baseline WAC Date:		1/1/14	N/A	N/A
Contract Year Start Date		7/1/14	N/A	N/A

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price.

5.3.1 (b) (Effective 7/1/2015 through 12/31/2015)

Manufacturer Drug Name: Apidra				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 1	57%	N/A	N/A
Administrative Fee		3%	N/A	N/A
Price Protection factor		N/A	N/A	N/A
Baseline WAC Date:		N/A	N/A	N/A
Contract Year Start Date		N/A	N/A	N/A

Conditions to Rebate for Rebate Tables 5.3(a) Lantus and 5.3(b) Apidra:

1. All NDC's of Manufacturer Drug are on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing; provided that Drugs manufactured, marketed or distributed by one manufacturer in the Defined Drug Market will be considered as one Drug. All other competitive Drugs within the Defined Drug Market are not listed on Formulary and are not covered; and
2. Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus and Apidra shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus and Apidra vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus and Apidra pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' and Apidra's Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Lantus' and Apidra's Defined Drug Market are subject to quantity limit consistent with their respective package inserts.

5.3.2 Only for Benefit Contracts with less than three and one-half (3.5) million Consumers

5.3.2 (a) (Effective 1/1/2016 through 12/31/2017)

Manufacturer Drug Name: Lantus*				
Benefit Design:	**Formulary**	**Highly**	**Managed**	**Covered**

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	Status	Managed		
Base Rebate Rate %	1 of 1	43%*	N/A	N/A
Administrative Fee		3%	N/A	N/A
Price Protection factor		7%	N/A	N/A
Baseline WAC Date:		1/1/14	N/A	N/A
Contract Year Start Date		7/1/14	N/A	N/A

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price.

5.3.2 (b) (Effective 1/1/2016 through 12/31/2017)

Manufacturer Drug Name: Apidra				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 1	57%	N/A	N/A
Administrative Fee		3%	N/A	N/A
Price Protection factor		N/A	N/A	N/A
Baseline WAC Date:		N/A	N/A	N/A
Contract Year Start Date		N/A	N/A	N/A

Conditions to Rebate for Rebate Tables 5.3(a) Lantus and 5.3(b) Apidra:

1. All NDC's of Manufacturer Drug are on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing; provided that Drugs manufactured, marketed or distributed by one manufacturer in the Defined Drug Market will be considered as one Drug. All other competitive Drugs within the Defined Drug Market are not listed on Formulary and are not covered; and
2. Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus and Apidra shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus and Apidra vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus and Apidra pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' and Apidra's Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Lantus' and Apidra's Defined Drug Market are subject to quantity limit consistent with their respective package inserts.

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[redacted]

6. Rebate Terms – QRPDP and utilization ineligible for Administrative Fees per Section 3 of this Exhibit A (other than Managed Medicaid and CHIP).

6.1 PREFERRED

Option A (Effective 7/1/2015 through 6/30/2017):

Manufacturer Drug Name: Lantus*			
Benefit Design:	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	45%*	n/a	n/a
Administrative Fee	0%	n/a	n/a
Price Protection factor	7%	n/a	n/a
Baseline WAC Date:	1/1/14	n/a	n/a
Contract Year Start Date	7/1/14	n/a	n/a

*The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative

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Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6 ("Best Price").

Conditions to Rebate:

1. All NDC's of Manufacturer Drug are on Formulary with Unrestricted Access in tier 1, 2 or 3 as of the date of dispensing. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Lantus' Defined Drug Market are subject to quantity limit consistent with their respective package inserts; and
2. A certain package form of Lantus may be disadvantaged to one (1) comparable package form of another Drug in Lantus' Defined Drug Market, provided all Lantus package forms are still listed and adjudicated with Unrestricted Access in accordance with Condition 1 above. In the event that a package form of Lantus is disadvantaged to more than one (1) comparable package form, all NDC's of Lantus, i.e. both vial and pen, shall be ineligible for Rebates as of such date of dispensing. The following examples are provided for clarification of rebate eligibility and not to be considered an exhaustive list:

Would Pay Vial and Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	3	Non-preferred	3	Non-preferred
Levemir	Vial	1	Preferred	1	Preferred
Comp #3	Vial	3	Non-preferred	3	Non-preferred
Lantus	Pen	3	Non-preferred	3	Non-preferred
Levemir	Pen	1	Preferred	3	Non-preferred
Comp #3	Pen	3	Non-preferred	2	Preferred

Would **NOT** Pay Vial or Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	3	Non-preferred	3	Non-preferred
Levemir	Vial	1	Preferred	1	Preferred
Comp #3	Vial	2	Preferred	3	Non-preferred
Lantus	Pen	3	Non-preferred	3	Non-preferred
Levemir	Pen	1	Preferred	1	Preferred
Comp #3	Pen	2	Preferred	2	Preferred

Option B (Effective 7/1/2015 through 6/30/2017):

Manufacturer Drug Name: Lantus*				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 2	n/a	15%*	10%*
Administrative Fee		n/a	0%	0%
Price Protection factor		n/a	7%	7%
Baseline WAC Date:		n/a	1/1/14	1/1/14
Contract Year Start Date		n/a	7/1/14	7/1/14

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* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price.

Conditions to Rebate:

1. All NDC's of Manufacturer Drug were on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing; and
2. A Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Lantus' Defined Drug Market are subject to quantity limit consistent with their respective package inserts; and
3. No package form of Lantus will be disadvantaged to a comparable package form of any other Drug in Lantus' Defined Drug Market. In the event that a package form of Lantus is disadvantaged to a comparable package form, all NDC's of Lantus, both vial and pen, shall be ineligible for Rebates as of such date of dispensing. The following examples are provided for clarification of Rebate eligibility and not to be considered an exhaustive list:

Would Pay Vial and Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	1	Preferred	1	Preferred
Levemir	Vial	1	Preferred	1	Preferred
Lantus	Pen	1	Preferred	2	Preferred
Levemir	Pen	1	Preferred	2	Preferred

Would **NOT** Pay Vial or Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	1	Preferred	2	Preferred
Levemir	Vial	1	Preferred	1	Preferred
Lantus	Pen	3	Non-preferred	2	Preferred
Levemir	Pen	3	Non-preferred	2	Preferred

6.2 PREFERRED

6.2(a) (Effective 7/1/2015 through 6/30/2017)

Manufacturer Drug Name: Apidra				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 2 or less	50%	50%	50%
Rebate %	1 of 3	45%	45%	45%
Administrative Fee		0%	0%	0%
Price Protection		n/a	n/a	n/a

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factor				
Baseline WAC Date:		n/a	n/a	n/a

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6.3 PREFERRED – EXCLUSION

6.3.1 Only for Benefit Contracts with less than three and one-half (3.5) million Consumers.

6.3.1 (a) (Effective 1/1/2016 through 6/30/2017)

Manufacturer Drug Name: Lantus*				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 1	46%*	N/A	N/A
Administrative Fee		0%	N/A	N/A
Price Protection factor		7%	N/A	N/A
Baseline WAC Date:		1/1/14	N/A	N/A
Contract Year Start Date		7/1/14	N/A	N/A

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price.

6.3.1 (b) (Effective 1/1/2016 through 6/30/2017)

Manufacturer Drug Name: Apidra				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 1	60%	N/A	N/A
Administrative Fee		0%	N/A	N/A
Price Protection factor		N/A	N/A	N/A
Baseline WAC Date:		N/A	N/A	N/A
Contract Year Start Date		N/A	N/A	N/A

Conditions to Rebate for Rebate Tables 6.3.1 (a) Lantus and 6.3.1 (b) Apidra:

1. All NDC's of Manufacturer Drug are on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing; provided that Drugs manufactured, marketed or distributed by one manufacturer in the Defined

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Drug Market will be considered as one Drug. All other competitive Drugs within the Defined Drug Market are not listed on Formulary and are not covered; and

2. Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus and Apidra shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus and Apidra vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus and Apidra pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' and Apidra's Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Lantus' and Apidra's Defined Drug Market are subject to quantity limit consistent with their respective package inserts.

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Manufacturer Drug Name: Lantus*		
	Formulary Status	**Managed Medicaid**
Base Rebate Rate %	1 of 2	5%*
Administrative Fee		0%
Price Protection factor		n/a
Baseline WAC Date:		n/a

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price.

[redacted]

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[redacted]

Conditions to Rebate for Rebate Tables 7.1 Lantus, [redacted]

1. Manufacturer Drug was on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing; and
2. A Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Lantus' Defined Drug Market are subject to quantity limit consistent with their respective package inserts; and
3. Notwithstanding the foregoing, the following Utilization Controls are permitted for the specifically identified Manufacturer Drug:

[redacted]

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[redacted]

7.6 (Effective 1/1/2016 through 12/31/16)

Manufacturer Drug Name: Toujeo		
Benefit Design:	**Formulary Status**	**Managed Medicaid**
Base Rebate Rate %	1 of 1	15%
Administrative Fee		0%
Price Protection factor		9.0%
Baseline WAC Date:		12/31/15

Conditions to Rebate for Rebate Tables 7.6 Toujeo:

1. All NDC's of Manufacturer Drug are on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing; provided that Drugs manufactured, marketed or distributed by one manufacturer in the Defined Drug Market will be considered as one Drug. All other competitive Drugs within the Defined Drug Market are not listed on Formulary and are not covered; and
2. Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting

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Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Toujeo shall not violate this condition: (i) a quantity limit of no more than 225mls per 3-month supply on Toujeo provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Toujeo's Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Toujeo's Defined Drug Market are subject to quantity limit consistent with their respective package inserts; and

3. Drugs within the Defined Drug Market must be subject to a step edit that requires the use of Toujeo for those Consumers who previously have never filled a prescription for Drugs within the Defined Drug Market.

7.7 (Effective 1/1/2017 through 12/31/17)

Manufacturer Drug Name: Toujeo		
Benefit Design:	**Formulary Status**	**Managed Medicaid**
Base Rebate Rate %	1 of 1	15%
Administrative Fee		0%
Price Predictability factor		9.0%
Baseline WAC Date:		12/31/16

Conditions to Rebate for Rebate Tables 7.7 Toujeo:

1. All NDC's of Toujeo are on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing. All other brand name Drugs within the Defined Drug Market are not listed on Formulary and are not covered; and
2. Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Toujeo shall not violate this condition: (i) a quantity limit of no more than 225mls per 3-month supply on Toujeo provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Toujeo's Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Toujeo's Defined Drug Market are subject to quantity limit consistent with their respective package inserts.

8. Rebate Terms – CHIP a stand-alone Federal healthcare program that operates independent from the Medicaid program as set forth in Article 2 Payment and Billing, Section 2.2.4

8.1 (Effective 7/1/2015 through 6/30/2017)

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Manufacturer Drug Name: Lantus*		
Benefit Design:	**Formulary Status**	**CHIP**
Base Rebate Rate %	1 of 2	45%*
Administrative Fee		0%
Price Protection factor		7%
Baseline WAC Date:		1/1/14
Contract Year Start Date		7/1/14

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price.

8.2 (Effective 7/1/2015 through 6/30/2017)

Manufacturer Drug Name: Apidra		
Benefit Design:	**Formulary Status**	**CHIP**
Base Rebate Rate %	1 of 2 or less	50%
Base Rebate Rate %	1 of 3	45%
Administrative Fee		0%
Price Protection factor		n/a
Baseline WAC Date:		n/a

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[redacted]

1. Manufacturer Drug was on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing; and
2. A Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus and Apidra shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus

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and Apidra vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus and Apidra pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' and Apidra's Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Lantus' and Apidra's Defined Drug Market are subject to quantity limit consistent with their respective package inserts; and

[redacted]

EXHIBIT D

DEFINED DRUG MARKET

MANUFACTURER DRUG	COMPETITIVE DRUG
Apidra® Apidra SoloStar®	Humalog Novolog Novolog FlexPen Humalog Kwik Pen
Toujeo SoloStar® Lantus® Lantus SoloStar®	Levemir Levemir FlexPen Levemir FlexTouch

[redacted]

SUPPLEMENTAL UTILIZATION DATA DRUG MARKET

MANUFACTURER DRUG	COMPETITIVE DRUG
Toujeo SoloStar® Lantus® Lantus SoloStar®	<u>Insulin</u> Humalog Mix 50/50 Humalog Mix 75/25 Humulin 50/50 Humulin 70/30 Humulin N Novolin Mix 70/30 Novolin N Novolog Mix 70/30 Relion Mix 70/30 Relion N [redacted]

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[redacted]

SIXTH (6TH) AMENDMENT TO THE
OPTUMRX, INC.
REBATE AGREEMENT

This SIXTH (6th) AMENDMENT TO THE OPTUMRX, INC. REBATE AGREEMENT ("Amendment"), dated as of December 15, 2015 ("Amendment Effective Date"), is made and entered into by and between, sanofi-aventis U.S. LLC, on behalf of itself and its affiliate Genzyme Corporation, ("Manufacturer"), and OptumRx, Inc. ("Administrator"), on behalf of itself and its Contracting Payors, with reference to the following facts:

RECITALS

WHEREAS, Manufacturer and Administrator entered into that certain Rebate Agreement (as previously amended, the "Agreement"), with an effective date of January 1, 2013, providing, among other things, for Manufacturer to pay rebates to Administrator on units of certain Manufacturer Drugs; and

WHEREAS, Manufacturer and Administrator mutually desire to amend the Agreement as stated below.

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Manufacturer and Administrator hereby agree to amend the Agreement as follows:

1. Section 3.1.1 of the Agreement is hereby deleted in its entirety and replaced with the following new Section 3.1.1:

   3.1.1 To be eligible for a Rebate under this Agreement, a Manufacturer Drug must have been listed in all applicable electronic and printed publications except as otherwise stated in Exhibit A with respect to this Section 3.1.1, and must have been dispensed by a Provider for use by a Consumer pursuant to a Benefit Contract and in accordance with the terms and conditions of this Agreement, unless otherwise specified on Exhibit A.

2. Section 5.1 of the Agreement is hereby deleted in its entirety and replaced with the following new Section 5.1:

   5.1 Term. This Agreement shall become effective as of the Effective Date and shall remain in effect through December 31, 2019. Unless otherwise terminated as provided for herein, this Agreement shall renew for successive terms of twelve (12) months on the applicable anniversary of the Effective Date, upon the mutual written agreement of the parties.

3. Exhibit A Rebate and Administrative Fee Schedule of the Agreement is hereby deleted in its entirety and replaced with the following new Exhibit A Rebate and Administrative Fee Schedule attached hereto.

4. [redacted]

5. Effective January 1, 2016, Exhibit D Defined Drug Market of the Agreement is hereby deleted in its entirety and replaced with the following new Exhibit D Defined Drug Market attached hereto.

6. Effect of this Amendment. Capitalized terms used but not defined in this Amendment shall have the meanings ascribed to them in the Agreement. Except as otherwise amended by this Amendment, all other terms and conditions of the Agreement shall remain in full force and effect. In the event there is any inconsistency or conflict between the provisions in this Amendment and those in the Agreement, the provisions in this Amendment shall supersede and control.

IN WITNESS WHEREOF, Manufacturer and Administrator have executed this Amendment as of the date first written above.

ADMINISTRATOR

By: Robert C. Lahman

Name: Robert C. Lahman

Title: S.V.P., Industry Relations

Date: 2-3-2016

MANUFACTURER

By: [signature]

Name: Joseph Geremia

Title: Senior Director Contract Development

Date: 2-8-16

MANUFACTURER

By: [signature]

Name: Gregory Rubert

Title: Sr. Director Managment Reporting

Date: 2/8/16

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EXHIBIT A
REBATE AND ADMINISTRATIVE FEE SCHEDULE

1. Definitions

1.1 Benefit Design

i. "Covered" means a Benefit design that does not qualify as a Managed or Highly Managed Benefit design.

ii. "Managed" means a Benefit design characterized by a Formulary under which the Contracting Payor directly or indirectly influences availability or gives preference in dispensing decisions of Drugs in the same Defined Drug Market through monetary restrictions; for example, differential dollar Consumer co-payments for generic, branded Preferred and branded non-Preferred status as defined and determined by the Contracting Payor, where branded non-Preferred Drugs and branded Preferred Drugs have no less than an average co-payment differential of ten dollars ($10.00), or an equivalent co-insurance percentage differential.

iii. "Highly Managed" means a Benefit design characterized by a Formulary under which a Contracting Payor also has the ability, and in fact exercises such ability, to directly or indirectly influence availability or give preference in dispensing decisions of Drugs in the same Defined Drug Market through hard edit prior authorizations, NDC locks for non-Preferred Drugs, step edits, or other similar mechanisms where certain Drugs are intended to be more restricted in availability than other Preferred Drugs in the same Defined Drug Market.

1.2 "Formulary Status" means the position a Manufacturer Drug has on Formulary. A Formulary Status that is designated as 1 of [X] means that the Manufacturer Drug is 1 of [X] single-source branded Drugs in the Defined Drug Market with the applicable Formulary Status; provided that for the purpose of determining if this condition for Rebate has been met, line extensions of Drugs within the Manufacturer Drug's Defined Drug Market manufactured by the same manufacturer shall be considered as one Drug [redacted]

1.3 "Preferred" means (i) a Drug is covered by a Benefit and is adjudicated in the lowest copayment tier for branded Drugs for the applicable Defined Drug Market and where the copayment amount or coinsurance percentage for such Drug is lower than that of Drugs in the Defined Drug Market designated as "non-preferred", or (ii) a Drug is covered by a Benefit where the Drugs designated as "preferred" are covered by the Benefit and the Drugs excluded from Formulary or designated on Formulary as "non-preferred" or "excluded" are not covered by the Benefit or (iii) for Covered Benefit designs only, a Drug is covered by a Benefit where Drugs designated as "preferred" are covered by the Benefit and Manufacturer Drug is no more restricted in its availability than other branded Drugs in the same Defined Drug Market.

1.4 "Specialty Tier" means a separate category or tier of the Formulary designated for very high cost or unique Drugs. This term only applies with respect to Sections 5.2(e), 6.2(e), 7.4, and 8.6 for [redacted] and Sections 5.5, 6.5, 7.8, and 8.8 for [redacted]

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1.5 "Unrestricted Access" when referring to Lantus means a Manufacturer Drug is covered by a Benefit with no Utilization Controls. But when referring to all other Manufacturer Drugs, means a Manufacturer Drug covered by a Benefit with no Utilization Controls, except for the allowances set forth in 1.5 Utilization Controls.

1.6 "Utilization Controls" mean, unless such Utilization Controls applied are clinically appropriate in accordance with FDA labeling or indications and/or applied to all Drugs in the applicable Defined Drug Market, i) counter-detailing or counter-promoting, ii) switching or therapeutic substitution, iii) hard edit prior authorization, iv) NDC lock, v) step edit, and vi) quantity limit based upon package insert. For purposes of this definition, "Utilization Controls" excludes communications or education programs designed to encourage the use of generic Drugs, and any aspects of Administrator's or Contracting Payor's communication, website, or other activity whereby Consumers have access to or are made aware of prices of Drugs and/or the availability of over-the-counter products for purposes of managing Consumer cost sharing amounts.

2. Rebate Calculation

Rebates for each Manufacturer Drug will be based upon the Formulary status of the Manufacturer Drug at the time such Manufacturer Drug is dispensed. Rebates will be calculated on a per Unit dispensed basis. For each month, the Rebates for each Manufacturer Drug shall be calculated as follows:

Rebate = (Unit(s) of Manufacturer Drug) x (WAC) x (Total Rebate Rate for the applicable Manufacturer Drug)

3. <u>Administrative Fee</u>. The Administrative Fee rate is 3% for each Rebate eligible Unit of Manufacturer Drug The Administrative Fee shall not be charged on QRPDP, Managed Medicaid and CHIP utilization, and any other utilization where prohibited by Law. For each month, the Administrative Fee shall be calculated as follows:

Administrative Fee = (Unit(s) of Manufacturer Drug) x (WAC) x (Administrative Fee rate %)

4. <u>Protection of Rebate Amount</u>.

4.1 Price Protection.

This Section 4.1 is effective 12/15/15 through 12/31/15 for [redacted] (Sections 7.2) and Lantus (Section 5.3.1(a)).
This Section 4.1 is effective 12/15/15 through 6/30/17 for [redacted] (Sections 5.2(b), 6.2(b), and 8.3) and Lantus (Sections 5.1, 6.1, and 8.1).
This Section 4.1 is effective 1/1/16 through 6/30/17 for Lantus (Sections 5.3.2(a) 6.3.1(a)).

This Section 4.1 is effective 12/15/15 through 12/31/18 for [redacted] (Sections 5.4(a), 6.4(a), 7.5 and 8.7) and [redacted] Sections 5.5, 6.5, 7.8(a), and 8.8(a)).
This Section 4.1 is effective 1/1/16 through 12/31/19 for [redacted] (Sections 5.2(d), 6.2(d), and 8.5).
This Section 4.1 is effective 1/1/16 through 12/31/17 for [redacted] (Sections 5.2(e) and 6.2(e)).

Rebate rates are subject to automatic adjustment in the event the "WAC per Unit" for Manufacturer Drug is increased to a price that is greater than the "Allowed WAC per Unit" during any corresponding month of the Agreement. The initial "Allowed WAC per Unit" for a Manufacturer Drug is calculated by multiplying the "WAC per Unit" as of the date set forth in the Rebate terms below ("Baseline WAC Date") for the applicable Manufacturer Drug by (100% plus the "Price Protection" factor). The "Net WAC per Unit" is calculated by multiplying the "WAC per Unit" by (100% minus the Base Rebate Rate %). The "Base Rebate Rate %" is the Rebate percentage for the Manufacturer Drug set forth in the applicable Rebate tables below. The "Allowed WAC per Unit" for subsequent Contract Years is calculated by multiplying the "Allowed WAC" for the previous Contract Year by (100% plus the "Price Protection" factor). The initial Allowed WAC per Unit for a Manufacturer Drug will apply during the 12-month period following the Manufacturer Drug's Contract Year Start Date (which date is set forth in the Rebate terms below). Such initial 12-month period and each subsequent 12- month period is referred to as the applicable Manufacturer Drug's "Contract Year". The "Net Allowed WAC per Unit" is calculated by multiplying the "Allowed WAC per Unit" by (100% minus the Base Rebate Rate %). The "Price Protection" factor is set forth in the Rebate terms below for the applicable Manufacturer Drug. Effective as of the date the "WAC per Unit" first exceeds the "Allowed WAC per Unit" and continuing for the remainder of that Contract Year, subject to further adjustments in accordance with this Section 4.1 of this Exhibit A Rebate and Administrative Fee Schedule, an "Additional Rebate Rate" will be provided. The "Additional Rebate Rate" is calculated by determining the amount, if any, that the Current Net WAC Per Unit for a given month exceeds the Net Allowed WAC per Unit for the same month, divided by the then-current WAC per Unit. The resulting percentage is the "Additional Rebate Rate" and is added to the "Base Rebate Rate %" to produce a "Total Rebate Rate" that applies during that month. The Additional Rebate Rate will be paid each month in which the "Current Net WAC per Unit" exceeds the "Net Allowed WAC per Unit". The Additional Rebate Rate is re-calculated each month. For avoidance of doubt, the Total Rebate Rate calculation for [redacted] is subject to the terms of Section 2.2.6 Best Price. [redacted]

*The terms "Current Net WAC" and "Net Allowed WAC" are solely used for purposes to explain the calculation of price protection in this Agreement. These terms are not used outside of this Agreement and, furthermore, are not meant to define or describe any pricing terms of a Manufacturer Drug.

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EXAMPLE 1:

Price Protection factor:	6%			Year 1 Price increase 10%						Year 2 Price increase 10%						Year 3 Price increase 10%		
	Assumed WAC as of 12/31/2013	Jan. 2014	Feb. 2014	Mar. 15 2014		Dec. 2014		Jan. 2015	Feb. 2015	Mar. 2015		Dec. 2015		Jan. 2016	Feb. 2016	Mar. 2016		Dec. 2016
Current WAC/ Unit (Existing NDC)	6.00	6.00	6.00	6.60	→	6.60		6.60	6.60	7.26	→	7.26		7.26	7.26	7.99	→	7.99
Allowed WAC/ Unit (Existing NDC)		6.36	6.36	6.36		6.36	→	6.74	6.74	6.74		6.74	→	7.15	7.15	7.15		7.15
Current WAC/ Unit (New NDC)									6.60	7.26	→	7.26		7.26	7.26	7.99	→	7.99
Allowed WAC/ Unit (New NDC)									6.74	6.74		6.74	→	7.15	7.15	7.15		7.15
Current Net WAC / Unit		5.40	5.40	5.94		5.94		5.94	5.94	6.53		6.53		6.53	6.53	7.19		7.19
Net Allowed WAC / Unit	5.40	5.72	5.72	5.72		5.72		6.07	6.07	6.07		6.07		6.43	6.43	6.43		6.43
Additional Rebate :		$0.00	$0.00	$0.22		$0.22		$0.00	$0.00	$0.47		$0.47		$0.10	$0.10	$0.76		$0.76
Additional Rebate Rate:		0.0%	0.0%	3.3%		3.3%		0.0%	0.0%	6.4%		6.4%		1.4%	1.4%	9.5%		9.5%
Base Rebate Rate %:	10.0%	10.0%	10.0%	10.0%		10.0%		10.0%	10.0%	10.0%		10.0%		10.0%	10.0%	10.0%		10.0%
Total Rebate Rate	10.0%	10.0%	10.0%	13.3%	→	13.3%		10.0%	10.0%	16.4%	→	16.4%		11.4%	11.4%	19.5%	→	19.5%

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If a new NDC ("New NDC") matching the labeler code and product code ("9-digit National Drug Code" or "NDC-9") of a Manufacturer Drug covered by this Agreement comes into existence after the date that such Manufacturer Drug becomes covered by this Agreement, the Additional Rebate Rate for such New NDC(s) will be calculated consistent with the preceding paragraph except that (i) the Net Allowed WAC per Unit for the Existing NDCs (defined below) will apply to the New NDC(s) during each billing period and (ii) the Net WAC per Unit of such New NDC(s) will be adjusted to account for differences, if any, in days of therapy, unit size, strength, or similar factors, between the New NDC(s) and their corresponding Existing NDCs, which adjustment(s) the parties will work in good faith to establish. As used herein, the term "Existing NDCs" refers to the Manufacturer Drug NDC(s) covered by the Agreement on the day prior to the date that the applicable New NDC comes into existence that has the highest Net Allowed WAC per Unit; provided, however, that either party may elect for the Existing NDC to be the NDC that most closely resembles the New NDC with respect to days of therapy, unit size, strength, or similar factors, which the parties will mutually determine working together in good faith. Example 2 below demonstrates the Additional Rebate Rate calculation for a New NDC.

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EXAMPLE 2:

New NDC introduced Feb14, subject to same PP rate increase as current NDCs.
New NDC WAC normalized to Current NDC WAC, same Baseline WAC date.
Price Protection factor: 6%

	Assumed WAC as of 12/31/2012	Jan. 2013	Feb. 2013	Year 1 Price increase 10% Mar. 15 2013	Dec. 2013	Jan. 2014	Feb. 2014	Year 2 Price increase 10% Mar. 2014	Dec. 2014	Jan. 2015	Feb. 2015	Year 3 Price increase 10% Mar. 2015	Dec. 2015
Current WAC/ Unit (Current NDC)	6.00	6.00	6.00	6.60	6.60	6.60	6.60	7.26	7.26	7.26	7.26	7.99	7.99
Allowed WAC/ Unit (Current NDC)		6.36	6.36	6.36	6.36	6.74	6.74	6.74	6.74	7.15	7.15	7.15	7.15
Current WAC/ Unit (New NDC)							10.50	11.55	11.55	11.55	11.55	12.71	12.71
Current Normalized WAC/ Unit (New NDC)							9.90	10.89	10.89	10.89	10.89	11.98	11.98
Allowed WAC/ Unit (New NDC)							10.11	10.11	10.11	10.72	10.72	10.72	10.72
Current Net WAC / Unit (Current NDC)		5.40	5.40	5.94	5.94	5.94	5.94	6.53	6.53	6.53	6.53	7.19	7.19
Net Allowed WAC / Unit (Current NDC)	5.40	5.72	5.72	5.72	5.72	6.07	6.07	6.07	6.07	6.43	6.43	6.43	6.43
Current Net WAC / Unit (New NDC)							9.45	10.40	10.40	10.40	10.40	11.43	11.43
Net Allowed WAC / Unit (New NDC)							9.10	9.10	9.10	9.65	9.65	9.65	9.65
Additional Rebate (Current NDC) :		$0.00	$0.00	$0.22	$0.22	$0.00	$0.00	$0.47	$0.47	$0.10	$0.10	$0.76	$0.76
Additional Rebate Rate (Current NDC):		0.0%	0.0%	3.3%	3.3%	0.0%	0.0%	6.4%	6.4%	1.4%	1.4%	9.5%	9.5%
Additional Rebate (New NDC) :							$0.35	$1.29	$1.29	$0.75	$0.75	$1.79	$1.79
Additional Rebate Rate (New NDC):							3.3%	11.2%	11.2%	6.5%	6.5%	14.1%	14.1%
Base Rebate Rate %:	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%
Total Rebate Rate (Current NDC)	10.0%	10.0%	10.0%	13.3%	13.3%	10.0%	10.0%	16.4%	16.4%	11.4%	11.4%	19.5%	19.5%
Total Rebate Rate (New NDC)							13.3%	21.2%	21.2%	16.5%	16.5%	24.1%	24.1%

	Current WAC	DOT (can be changed to whatever the 'normalization' factor should be)	Normalized WAC / per DOT	WAC in effect for New NDC
Current NDC	6.60	60	0.11	
New NDC	10.50	90		9.90

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4.2 Price Protection

This section 4.2 is effective 12/15/15 through 12/31/15 for [redacted] (Sections 5.2(c), 6.2(c), 7.3 and 8.4).
This section 4.2 is effective 12/15/15 through 12/31/16 for [redacted] (Section 7.4)
This section 4.2 is effective 12/15/15 through 6/30/17 [redacted] (Section 8.6)
This section 4.2 is effective 1/1/16 through 12/31/16 for Toujeo (Section 7.6)
This section 4.2 is effective 1/1/17 through 12/31/17 for Toujeo (Section 7.7).

Rebate rates are subject to automatic adjustment in the event the "WAC per Unit" for Manufacturer Drug is increased to a price that is greater than the "Allowed WAC per Unit" during any corresponding month of the Agreement. The "Allowed WAC per Unit" for 2013 is calculated by multiplying the "WAC per Unit" as of the date set forth in the Rebate terms below ("Baseline WAC Date") for the applicable Manufacturer Drug by (100% plus the "Price Protection" factor). The "Net WAC per Unit" is calculated by multiplying the "WAC per Unit" by (100% minus the Base Rebate Rate %). The "Base Rebate Rate %" is the Rebate percentage for the Manufacturer Drug set forth in the Rebate tables below. The initial Allowed WAC per Unit for a Manufacturer Drug will apply during the 12-month period following the Agreement's Effective Date. Such initial 12-month period and each subsequent 12-month period is referred to as the applicable Manufacturer Drug's "Contract Year". The "Allowed WAC per Unit" for subsequent Contract Years is calculated by multiplying the "WAC per Unit" in effect for the applicable Manufacturer Drug on December 31 of the Contract Year immediately prior to the current Contract Year by (100% plus the "Price Protection" factor). The "Net Allowed WAC per Unit" is calculated by multiplying the "Allowed WAC per Unit" by (100% minus the Base Rebate Rate %). For avoidance of doubt: (a) the first pricing period shall be Contract Year 2013; (b) the second pricing period shall be Contract Year 2014; and (c) the third pricing period shall be Contract Year 2015. Price increases in one pricing period shall not be added to price increases in another pricing period for purposes of determining Additional Rebate Rates. The "Price Protection" factor is set forth in the Rebate terms below for the applicable Manufacturer Drug. Effective as of the date the "WAC per Unit" first exceeds the "Allowed WAC per Unit" and continuing for the remainder of that Contract Year, subject to further adjustments in accordance with this Section 4.2 of this Exhibit A Rebate and Administrative Fee Schedule, an "Additional Rebate Rate" will be provided. The "Additional Rebate Rate" is calculated by determining the amount, if any, that the Net WAC Per Unit for a given month exceeds the Net Allowed WAC per Unit for the same month, divided by the then-current WAC per Unit. The resulting percentage is the "Additional Rebate Rate" and is added to the "Base Rebate Rate %" to produce a "Total Rebate Rate" that applies during that month. The Additional Rebate Rate will be paid each month in which the "Current Net WAC Per Unit" exceeds the "Net Allowed WAC per Unit". The Additional Rebate Rate is re-calculated each month. For avoidance of doubt, the Total Rebate Rate calculation is subject to the terms of Section 2.2.6 Best Price. [redacted]

*The terms "Current Net WAC" and "Net Allowed WAC" are solely used for purposes to explain the calculation of price protection in this Agreement. These terms are not used outside of this Agreement and, furthermore, are not meant to define or describe any pricing terms of a Manufacturer Drug.

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EXAMPLE 1:

Price Protection factor:	6%			Year 1 Price increase 10%				Year 2 Price increase 10%			
	Assumed WAC as of 12/31/2012	Jan. 2013	Feb. 2013	Mar. 15 2013	Dec. 2013	Jan. 2014	Feb. 2014	Mar. 2014	Dec. 2014	Jan. 2015	Feb. 2015
Current WAC/ Unit (Existing NDC)	6.00	6.00	6.00	6.60	6.60	6.60	6.60	7.26	7.26	7.26	7.26
Allowed WAC/ Unit (Existing NDC)		6.36	6.36	6.36	6.36	7.00	7.00	7.00	7.00	7.70	7.70
Current WAC/ Unit (New NDC)							6.60	7.26	7.26	7.26	7.26
Allowed WAC/ Unit (New NDC)							7.00	7.00	7.00	7.70	7.70
Current Net WAC / Unit		5.40	5.40	5.94	5.94	5.94	5.94	6.53	6.53	6.53	6.53
Net Allowed WAC / Unit	5.40	5.72	5.72	5.72	5.72	6.30	6.30	6.30	6.30	6.93	6.93
Additional Rebate :		$0.00	$0.00	$0.22	$0.22	$0.00	$0.00	$0.24	$0.24	$0.00	$0.00
Additional Rebate Rate:		0.0%	0.0%	3.3%	3.3%	0.0%	0.0%	3.3%	3.3%	0.0%	0.0%
Base Rebate Rate %:	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%
Total Rebate Rate	10.0%	10.0%	10.0%	13.3%	13.3%	10.0%	10.0%	13.3%	13.3%	10.0%	10.0%

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If a new NDC ("New NDC") matching the labeler code and product code ("9-digit National Drug Code" or "NDC-9") of a Manufacturer Drug covered by this Agreement comes into existence after the date that such Manufacturer Drug becomes covered by this Agreement, the Additional Rebate Rate for such New NDC(s) will be calculated consistent with the preceding paragraph except that (i) the Net Allowed WAC per Unit for the Existing NDCs (defined below) will apply to the New NDC(s) during each billing period and (ii) the Net WAC per Unit of such New NDC(s) will be adjusted to account for differences, if any, in days of therapy, unit size, strength, or similar factors, between the New NDC(s) and their corresponding Existing NDCs, which adjustment(s) the parties will work in good faith to establish. As used herein, the term "Existing NDCs" refers to the Manufacturer Drug NDC(s) covered by the Agreement on the day prior to the date that the applicable New NDC comes into existence that has the highest Net Allowed WAC per Unit; provided, however, that either party may elect for the Existing NDC to be the NDC that most closely resembles the New NDC with respect to days of therapy, unit size, strength, or similar factors, which the parties will mutually determine working together in good faith. Example 2 below demonstrates the Additional Rebate Rate calculation for a New NDC.

EXAMPLE 2:

New NDC introduced Feb14, subject to same PP rate increase as Existing NDCs.
Same WAC/unit, same Baseline WAC date.
Price Protection factor: 6%

	Assumed WAC as of 12/31/2012	Jan. 2013	Feb. 2013	Year 1 Price increase 10% Mar. 15 2013	Dec. 2013	Allowed was 6.74 Jan. 2014	Feb. 2014	Year 2 Price increase 10% Mar. 2014	Dec. 2014	Jan. 2015	Feb. 2015
Current WAC/ Unit (Existing NDC)	6.00	6.00	6.00	6.60	6.60	6.60	6.60	7.26	7.26	7.26	7.26
Allowed WAC/ Unit (Existing NDC)		6.36	6.36	6.36	6.36	7.00	7.00	7.00	7.00	7.70	7.70
Current WAC/ Unit (New NDC)							10.50	11.55	11.55	11.55	11.55
Current Normalized WAC/ Unit (New NDC)							9.90	10.89	10.89	10.89	10.89
Allowed WAC/ Unit (New NDC)							10.49	10.49	10.49	12.24	12.24
Current Net WAC / Unit (Existing NDC)		5.40	5.40	5.94	5.94	5.94	5.94	6.53	6.53	6.53	6.53
Net Allowed WAC / Unit (Existing NDC)	5.40	5.72	5.72	5.72	5.72	6.30	6.30	6.30	6.30	6.93	6.93
Current Net WAC / Unit (New NDC)							9.45	10.40	10.40	10.40	10.40
Net Allowed WAC / Unit (New NDC)							9.44	9.44	9.44	11.02	11.02
Additional Rebate (Existing NDC):		$0.00	$0.00	$0.22	$0.22	$0.00	$0.00	$0.24	$0.24	$0.00	$0.00
Additional Rebate Rate (Existing NDC):		0.0%	0.0%	3.3%	3.3%	0.0%	0.0%	3.3%	3.3%	0.0%	0.0%
Additional Rebate (New NDC) :							$0.01	$0.95	$0.95	$0.00	$0.00
Additional Rebate Rate (New NDC):							0.1%	8.2%	8.2%	0.0%	0.0%
Base Rebate Rate %:	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%
Total Rebate Rate (Existing NDC)	10.0%	10.0%	10.0%	13.3%	13.3%	10.0%	10.0%	13.3%	13.3%	10.0%	10.0%
Total Rebate Rate (New NDC)							10.1%	18.2%	18.2%	10.0%	10.0%

	Current WAC	DOT (can be changed to whatever the 'normalization' factor should be)	Normalized WAC / per DOT	WAC in effect for New NDC
Existing NDC	6.60	60	0.11	
New NDC	10.50	90		9.90

5. Rebate Terms – non-QRPDP, non-Managed Medicaid and non-CHIP

5.1 PREFERRED

Option A: (Effective 12/15/2015 through 6/30/2017)

Manufacturer Drug Name: Lantus*			
Benefit Design:	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	42%*	n/a	n/a
Administrative Fee	3%	n/a	n/a
Price Protection factor	7%	n/a	n/a
Baseline WAC Date:	1/1/14	n/a	n/a
Contract Year Start Date	7/1/14	n/a	n/a

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price.

Conditions to Rebate:

1. All NDC's of Manufacturer Drug are on Formulary with Unrestricted Access in tier 1, 2 or 3 as of the date of dispensing. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Lantus' Defined Drug Market are subject to quantity limit consistent with their respective package inserts; and

2. A certain package form of Lantus may be disadvantaged to one (1) comparable package form of another Drug in Lantus' Defined Drug Market, provided all Lantus package forms are still listed and adjudicated with Unrestricted Access in accordance with Condition 1 above. In the event that a package form of Lantus is disadvantaged to more than one (1) comparable package form, all NDC's of Lantus, i.e. both vial and pen, shall be ineligible for Rebates as of such date of dispensing. The following examples are provided for clarification of rebate eligibility and not to be considered an exhaustive list:

Would Pay Vial and Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	3	Non-preferred	3	Non-preferred
Levemir	Vial	1	Preferred	1	Preferred
Comp #3	Vial	3	Non-preferred	3	Non-preferred
Lantus	Pen	3	Non-preferred	3	Non-preferred
Levemir	Pen	1	Preferred	3	Non-preferred
Comp #3	Pen	3	Non-preferred	2	Preferred

Would **NOT** Pay Vial or Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	3	Non-preferred	3	Non-preferred
Levemir	Vial	1	Preferred	1	Preferred
Comp #3	Vial	2	Preferred	3	Non-preferred
Lantus	Pen	3	Non-preferred	3	Non-preferred
Levemir	Pen	1	Preferred	1	Preferred
Comp #3	Pen	2	Preferred	2	Preferred

Option B: (Effective 12/15/2015 through 6/30/2017)

Manufacturer Drug Name: Lantus*				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 2	n/a	12%*	7%*
Administrative Fee		n/a	3%	3%
Price Protection factor		n/a	7%	7%
Baseline WAC Date:		n/a	1/1/14	1/1/14
Contract Year Start Date		n/a	7/1/14	7/1/14

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6,Best Price.

Conditions to Rebate:

1. All NDC's of Manufacturer Drug are on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing; and

2. Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Lantus' Defined Drug Market are subject to quantity limit consistent with their respective package inserts; and

3. No package form of Lantus will be disadvantaged to a comparable package form of any other Drug in Lantus' Defined Drug Market. In the event that a package form of Lantus is disadvantaged to a comparable package form, all NDC's of Lantus, i.e. both vial and pen, shall be ineligible for Rebates as of such date of dispensing. The following examples

are provided for clarification of Rebate eligibility and not to be considered an exhaustive list:

Would Pay Vial and Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	1	Preferred	1	Preferred
Levemir	Vial	1	Preferred	1	Preferred
Lantus	Pen	1	Preferred	2	Preferred
Levemir	Pen	1	Preferred	2	Preferred

Would **NOT** Pay Vial or Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	1	Preferred	2	Preferred
Levemir	Vial	1	Preferred	1	Preferred
Lantus	Pen	3	Non-preferred	2	Preferred
Levemir	Pen	3	Non-preferred	2	Preferred

5.2 PREFERRED

5.2(a) Effective 12/15/2015 through 6/30/2017)

Manufacturer Drug Name: Apidra				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 2 or less	47%	47%	47%
Base Rebate Rate %	1 of 3	42%	42%	42%
Administrative Fee		3%	3%	3%
Price Protection factor		n/a	n/a	n/a
Baseline WAC Date:		n/a	n/a	n/a

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5.3 PREFERRED – EXCLUSION

5.3.1 Only for Benefit Contracts with less than two (2) million Consumers

5.3.1 (a) (Effective 12/15/2015 through 12/31/2015)

Manufacturer Drug Name: Lantus*				
Benefit Design:	Formulary Status	Highly Managed	Managed	Covered

Base Rebate Rate %	1 of 1	43%*	N/A	N/A
Administrative Fee		3%	N/A	N/A
Price Protection factor		7%	N/A	N/A
Baseline WAC Date:		1/1/14	N/A	N/A
Contract Year Start Date		7/1/14	N/A	N/A

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price.

5.3.1 (b) (Effective 12/15/2015 through 12/31/2015)

Manufacturer Drug Name: Apidra				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 1	57%	N/A	N/A
Administrative Fee		3%	N/A	N/A
Price Protection factor		N/A	N/A	N/A
Baseline WAC Date:		N/A	N/A	N/A
Contract Year Start Date		N/A	N/A	N/A

Conditions to Rebate for Rebate Tables 5.3(a) Lantus and 5.3(b) Apidra:

1. All NDC's of Manufacturer Drug are on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing; provided that Drugs manufactured, marketed or distributed by one manufacturer in the Defined Drug Market will be considered as one Drug. All other competitive Drugs within the Defined Drug Market are not listed on Formulary and are not covered; and

2. Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus and Apidra shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus and Apidra vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus and Apidra pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' and Apidra's Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Lantus' and Apidra's Defined Drug Market are subject to quantity limit consistent with their respective package inserts.

5.3.2 Only for Benefit Contracts with less than three and one-half (3.5) million Consumers

5.3.2 (a) (Effective 1/1/2016 through 6/30/2017)

Manufacturer Drug Name: Lantus*				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 1	43%*	N/A	N/A
Administrative Fee		3%	N/A	N/A
Price Protection factor		7%	N/A	N/A
Baseline WAC Date:		1/1/14	N/A	N/A
Contract Year Start Date		7/1/14	N/A	N/A

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price.

5.3.2 (b) (Effective 1/1/2016 through 12/31/2017)

Manufacturer Drug Name: Apidra				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 1	57%	N/A	N/A
Administrative Fee		3%	N/A	N/A
Price Protection factor		N/A	N/A	N/A
Baseline WAC Date:		N/A	N/A	N/A
Contract Year Start Date		N/A	N/A	N/A

Conditions to Rebate for Rebate Tables 5.3(a) Lantus and 5.3(b) Apidra:

1. All NDC's of Manufacturer Drug are on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing; provided that Drugs manufactured, marketed or distributed by one manufacturer in the Defined Drug Market will be considered as one Drug. All other competitive Drugs within the Defined Drug Market are not listed on Formulary and are not covered; and

2. Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus and Apidra shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus and Apidra vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus and Apidra pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' and Apidra's Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided

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all brand name Drugs in Lantus' and Apidra's Defined Drug Market are subject to quantity limit consistent with their respective package inserts.

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6. Rebate Terms – QRPDP and utilization ineligible for Administrative Fees per Section 3 of this Exhibit A (other than Managed Medicaid and CHIP).

6.1 PREFERRED

Option A (Effective 12/15/2015 through 6/30/2017):

Manufacturer Drug Name: Lantus*			
Benefit Design:	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	45%*	n/a	n/a
Administrative Fee	0%	n/a	n/a
Price Protection factor	7%	n/a	n/a
Baseline WAC Date:	1/1/14	n/a	n/a
Contract Year Start Date	7/1/14	n/a	n/a

*The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6 ("Best Price").

Conditions to Rebate:

1. All NDC's of Manufacturer Drug are on Formulary with Unrestricted Access in tier 1, 2 or 3 as of the date of dispensing. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided

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all brand name Drugs in Lantus' Defined Drug Market are subject to quantity limit consistent with their respective package inserts; and

2. A certain package form of Lantus may be disadvantaged to one (1) comparable package form of another Drug in Lantus' Defined Drug Market, provided all Lantus package forms are still listed and adjudicated with Unrestricted Access in accordance with Condition 1 above. In the event that a package form of Lantus is disadvantaged to more than one (1) comparable package form, all NDC's of Lantus, i.e. both vial and pen, shall be ineligible for Rebates as of such date of dispensing. The following examples are provided for clarification of rebate eligibility and not to be considered an exhaustive list:

Would Pay Vial and Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	3	Non-preferred	3	Non-preferred
Levemir	Vial	1	Preferred	1	Preferred
Comp #3	Vial	3	Non-preferred	3	Non-preferred
Lantus	Pen	3	Non-preferred	3	Non-preferred
Levemir	Pen	1	Preferred	3	Non-preferred
Comp #3	Pen	3	Non-preferred	2	Preferred

Would **NOT** Pay Vial or Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	3	Non-preferred	3	Non-preferred
Levemir	Vial	1	Preferred	1	Preferred
Comp #3	Vial	2	Preferred	3	Non-preferred
Lantus	Pen	3	Non-preferred	3	Non-preferred
Levemir	Pen	1	Preferred	1	Preferred
Comp #3	Pen	2	Preferred	2	Preferred

Option B (Effective 12/15/2015 through 6/30/2017):

Manufacturer Drug Name: Lantus*				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 2	n/a	15%*	10%*
Administrative Fee		n/a	0%	0%
Price Protection factor		n/a	7%	7%
Baseline WAC Date:		n/a	1/1/14	1/1/14
Contract Year Start Date		n/a	7/1/14	7/1/14

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price.

Conditions to Rebate:

1. All NDC's of Manufacturer Drug were on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing; and

2. A Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus pen provided there is

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an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Lantus' Defined Drug Market are subject to quantity limit consistent with their respective package inserts; and

3. No package form of Lantus will be disadvantaged to a comparable package form of any other Drug in Lantus' Defined Drug Market. In the event that a package form of Lantus is disadvantaged to a comparable package form, all NDC's of Lantus, both vial and pen, shall be ineligible for Rebates as of such date of dispensing. The following examples are provided for clarification of Rebate eligibility and not to be considered an exhaustive list:

Would Pay Vial and Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	1	Preferred	1	Preferred
Levemir	Vial	1	Preferred	1	Preferred
Lantus	Pen	1	Preferred	2	Preferred
Levemir	Pen	1	Preferred	2	Preferred

Would NOT Pay Vial or Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	1	Preferred	2	Preferred
Levemir	Vial	1	Preferred	1	Preferred
Lantus	Pen	3	Non-preferred	2	Preferred
Levemir	Pen	3	Non-preferred	2	Preferred

6.2 PREFERRED

6.2(a) (Effective 12/15/2015 through 6/30/2017)

Manufacturer Drug Name: Apidra				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 2 or less	50%	50%	50%
Rebate %	1 of 3	45%	45%	45%
Administrative Fee		0%	0%	0%
Price Protection factor		n/a	n/a	n/a
Baseline WAC Date:		n/a	n/a	n/a

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6.3 PREFERRED – EXCLUSION

6.3.1 Only for Benefit Contracts with less than three and one-half (3.5) million Consumers.

6.3.1 (a) (Effective 1/1/2016 through 6/30/2017)

Manufacturer Drug Name: Lantus*				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 1	46%*	N/A	N/A
Administrative Fee		0%	N/A	N/A
Price Protection factor		7%	N/A	N/A
Baseline WAC Date:		1/1/14	N/A	N/A
Contract Year Start Date		7/1/14	N/A	N/A

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price.

6.3.1 (b) (Effective 1/1/2016 through 6/30/2017)

Manufacturer Drug Name: Apidra				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 1	60%	N/A	N/A
Administrative Fee		0%	N/A	N/A
Price Protection factor		N/A	N/A	N/A
Baseline WAC Date:		N/A	N/A	N/A
Contract Year Start Date		N/A	N/A	N/A

Conditions to Rebate for Rebate Tables 6.3.1 (a) Lantus and 6.3.1 (b) Apidra:

1. All NDC's of Manufacturer Drug are on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing; provided that Drugs manufactured, marketed or distributed by one manufacturer in the Defined Drug Market will be considered as one Drug. All other competitive Drugs within the Defined Drug Market are not listed on Formulary and are not covered; and

2. Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Lantus and Apidra shall not violate this condition: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus and Apidra vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus and Apidra pen provided there is an exception

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process for such quantity limit when an exception is medically necessary and all brand name Drugs in Lantus' and Apidra's Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Lantus' and Apidra's Defined Drug Market are subject to quantity limit consistent with their respective package inserts.

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7. Rebate Terms - Managed Medicaid.

7.1 Lantus (Effective 12/15/2015 through 12/31/2015)

Manufacturer Drug Name: Lantus*		
	Formulary Status	**Managed Medicaid**
Base Rebate Rate %	1 of 2	5%*
Administrative Fee		0%
Price Protection factor		n/a
Baseline WAC Date:		n/a

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price.

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7.6 (Effective 1/1/2016 through 12/31/16)

Manufacturer Drug Name: Toujeo		
Benefit Design:	**Formulary Status**	**Managed Medicaid**
Base Rebate Rate %	1 of 1	15%
Administrative Fee		0%
Price Protection factor		9.0%
Baseline WAC Date:		12/31/15

Conditions to Rebate for Rebate Tables 7.6 Toujeo:

1. All NDC's of Manufacturer Drug are on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing; provided that Drugs manufactured, marketed or distributed by one manufacturer in the Defined Drug Market will be considered as one Drug. All other competitive Drugs within the Defined Drug Market are not listed on Formulary and are not covered; and
2. Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Toujeo shall not violate this condition: (i) a quantity limit of no more than 225mls per 3-month supply on Toujeo provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Toujeo's Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Toujeo's Defined Drug Market are subject to quantity limit consistent with their respective package inserts; and
3. Drugs within the Defined Drug Market must be subject to a step edit that requires the use of Toujeo for those Consumers who previously have never filled a prescription for Drugs within the Defined Drug Market.

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7.7 (Effective 1/1/2017 through 12/31/17)

Manufacturer Drug Name: Toujeo		
Benefit Design:	**Formulary Status**	**Managed Medicaid**
Base Rebate Rate %	1 of 1	15%
Administrative Fee		0%
Price Predictability factor		9.0%
Baseline WAC Date:		12/31/16

Conditions to Rebate for Rebate Tables 7.7 Toujeo:

1. All NDC's of Toujeo are on Formulary with Preferred status and the applicable Formulary Status in the table above as of the date of dispensing. All other brand name Drugs within the Defined Drug Market are not listed on Formulary and are not covered; and
2. Manufacturer Drug was not disadvantaged as compared to other brand name Drugs within the Defined Drug Market with regard to Administrator's or Contracting Payor's Utilization Controls. Notwithstanding the foregoing, imposition of any of the following quantity limit requirements on Toujeo shall not violate this condition: (i) a quantity limit of no more than 225mls per 3-month supply on Toujeo provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in Toujeo's Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in Toujeo's Defined Drug Market are subject to quantity limit consistent with their respective package inserts.

[redacted]

[redacted]

[redacted]

8. Rebate Terms – CHIP a stand-alone Federal healthcare program that operates independent from the Medicaid program as set forth in Article 2 Payment and Billing, Section 2.2.4

8.1 (Effective 12/15/2015 through 6/30/2017)

Manufacturer Drug Name: Lantus*		
Benefit Design:	**Formulary Status**	**CHIP**
Base Rebate Rate %	1 of 2	45%*
Administrative Fee		0%
Price Protection factor		7%
Baseline WAC Date:		1/1/14
Contract Year Start Date		7/1/14

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price.

8.2 (Effective 12/15/2015 through 6/30/2017)

Manufacturer Drug Name: Apidra		
Benefit Design:	**Formulary Status**	**CHIP**
Base Rebate Rate %	1 of 2 or less	50%
Base Rebate Rate %	1 of 3	45%
Administrative Fee		0%
Price Protection factor		n/a
Baseline WAC Date:		n/a

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[redacted]

[redacted]

[redacted]

General Rebate Criteria

This Section 8.8 is applicable to all Options in Section 8.8 of this Exhibit A. Manufacturer Drug may be subject to a prior authorization and such prior authorization shall not render the applicable utilization ineligible for Rebates or Administrative Fees so long as such prior authorization (or a modified version of such prior authorization that reflects clinically appropriate differences in FDA labeling or published clinical guidelines) is applied to all Drugs in Manufacturer Drug's Defined Drug Market.

Notwithstanding the foregoing, if a Benefit Contract subjects [redacted] utilization to a prior authorization program that contains or is more restrictive than the following criteria, such utilization is not eligible for Rebates:

ii. For patients with Atherosclerotic cardiovascular disease (ASCVD) (with or without heterozygous familial hypercholesterolemia (HeFH)) on a maximally tolerated lipid-lowering regimen, the requirement of an LDL-C threshold of more than 100 mg/dl.

ii. For patients with HeFH without ASCVD, on a maximally tolerated lipid-lowering regimen, the requirement of an LDL-C threshold of more than 130 mg/dl.

iii. As it relates to trial of other lipid lowering products, requirement of more than the following:

a. 12 week trial of maximally tolerated statin intensity (may require more than one statin trial to determine maximally tolerated intensity); and
b. 12 week trial of [redacted] or bile acid sequestrant.

Nothing in this section is intended to contradict FDA labeling or published clinical guidelines. If FDA labeling or clinical guidelines are updated to support criteria more restrictive than outlined above for the Defined Drug Market, prior authorization programs that include such criteria would be eligible for the Rebates and Administrative Fees outlined in this Amendment notwithstanding the inclusion of such criteria, provided such criteria is applied to all Drugs in Manufacturer Drug's Defined Drug Market.

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[redacted]

EXHIBIT D
DEFINED DRUG MARKET

MANUFACTURER DRUG	COMPETITIVE DRUG
Apidra® Apidra SoloStar®	Humalog Novolog Novolog FlexPen Humalog Kwik Pen
Toujeo SoloStar® Lantus® Lantus SoloStar®	Levemir Levemir FlexPen Levemir FlexTouch

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SUPPLEMENTAL UTILIZATION DATA DRUG MARKET

MANUFACTURER DRUG	COMPETITIVE DRUG	
Toujeo SoloStar® Lantus® Lantus SoloStar®	Insulin Humalog Mix 50/50 Humalog Mix 75/25 Humulin 50/50 Humulin 70/30 Humulin N Novolin Mix 70/30 Novolin N Novolog Mix 70/30 Relion Mix 70/30 Relion N Ryzodeg 70/30 Tresiba++ Levemir Levemir FlexPen Levemir FlexTouch	[redacted]

[redacted]

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FOURTEENTH AMENDMENT TO THE REBATE AGREEMENT

This FOURTEENTH AMENDMENT TO THE REBATE AGREEMENT ("Amendment"), dated as of January 1, 2019 ("Amendment Effective Date"), is made and entered into by and between sanofi-aventis U.S. LLC, on behalf of itself and its affiliate Genzyme Corporation, ("Manufacturer") and OptumRx, Inc. ("Administrator"), on behalf of itself and its Contracting Payors, with reference to the following facts:

RECITALS

WHEREAS, Manufacturer and Administrator entered into that certain Rebate Agreement (as previously amended, the "Agreement"), with an effective date of January 1, 2013, providing, among other things, for Manufacturer to pay Rebates to Administrator on units of certain Manufacturer Drugs; and

WHEREAS, Manufacturer and Administrator mutually desire to amend the Agreement as stated below.

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Manufacturer and Administrator hereby agree to amend the Agreement as follows:

1. Effect of this Amendment. Capitalized terms used but not defined in this Amendment shall have the meanings ascribed to them in the Agreement. Except as otherwise amended by this Amendment, all other terms and conditions of the Agreement shall remain in full force and effect. In the event there is any inconsistency or conflict between the provisions in this Amendment and those in the Agreement, the provisions in this Amendment shall supersede and control.

2. Section 1.17 is hereby deleted in its entirety and replaced as follows:

   1.17 "Provider" means any licensed prescriber or, licensed pharmacy, that is eligible to dispense Drugs to Consumers in accordance with the applicable Benefit Contract requirements and that has a valid National Provider Identifier (NPI) or National Council for Prescription Drug Programs (NCPDP) number. The term Provider does not include any pharmacy located outside of the United States, institutional pharmacy or government-owned pharmacy.

3. Sections 1.25 and 1.26 are hereby added to the Agreement as follows:

   1.25 "Rebate Sharing Program" means a program administered by Administrator on behalf of Contracting Payors pursuant to which a portion of Rebates are shared with Consumers to reduce the Consumer's share of a Drug's cost.

1.26 "Utilization Controls" mean, unless such Utilization Controls applied are clinically appropriate in accordance with FDA labeling or indications and/or applied to all Drugs in the applicable Defined Drug Market, i) counter-detailing or counter-promoting, ii) switching or therapeutic substitution, iii) hard edit prior authorization, iv) NDC lock, v) step edit, and (vi) a quantity limit more restrictive than a Drug's package insert. For purposes of this definition, "Utilization Controls" excludes communications or education programs designed to encourage the use of generic Drugs, and any aspects of Administrator's or Contracting Payor's communication, website, or other activity whereby Consumers have access to or are made aware of prices of Drugs and/or the availability of over-the-counter products for purposes of managing Consumer cost sharing amounts.

4. Romanettes (vi) and (vii) are hereby added to Section 2.5 of the Agreement as follows:

(vi) if there is a material shortage or public health and/or other material safety concern impacting the availability of a Manufacturer Drug ("Shortage"), then beginning on the date provided in such notice that Administrator is required to provide to Manufacturer (as set forth below) and continuing through the first date following the end of such impacted availability on which the applicable Benefit Contract is reasonably capable of reversing the Formulary and Utilization Control changes made in response to such impacted availability, a Benefit Contract may place additional Drugs on the co-payment amount or co-insurance percentage tier on which such Manufacturer Drug is positioned, or remove Utilization Controls from Drugs in Manufacturer Drug's Defined Drug Market, without losing eligibility for the Rebate rate that such Benefit Contract would have been entitled to in the absence of such Formulary and/or Utilization Control changes, provided that (a) if any Contracting Payor elects to modify its Formulary or utilization management protocols in response to such Shortage, Administrator shall notify Manufacturer of such Shortage and specify the date that Contracting Payor(s) will be making Formulary and/or Utilization Control changes and (b) if Manufacturer reasonably disputes the existence of the Shortage on which such Formulary and/or Utilization Control changes were based, Manufacturer retains its right to dispute applicable portions of Rebate invoices in accordance with Section 2.2.3; and (vii) any impact to a Consumer's cost sharing obligation (e.g., co-payment amount, co-insurance percentage, or other patient cost responsibility) resulting from the implementation of a Rebate Sharing Program will not be taken into account when determining whether a Benefit Contract has satisfied applicable Rebate conditions set forth in Exhibit A and the implementation of a Rebate Sharing Program involving a Manufacturer Drug may cause Consumers to be aware that a Rebate relationship exists between Administrator and Manufacturer.

5. Section 5.1 of the Agreement is hereby deleted in its entirety and replaced by the following new Section 5.1:

5.1 Term. This Agreement shall become effective as of the Effective Date and shall remain in effect through **December 31, 2022.** Unless otherwise terminated as provided for herein, this Agreement shall renew for successive terms of twelve (12) months on the

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applicable anniversary of the Effective Date, upon the mutual written agreement of the parties.

6. Section 4.6 of the Agreement is hereby deleted in its entirety and replaced by the following new Section 4.6:

4.6 Regulatory Compliance.

4.6.1 The Rebates received under this Agreement may represent discounts within the meaning of Section 1128B(b) of the Social Security Act and its implementing regulations (42 C.F.R. § 1001.952) which shall be fully and accurately disclosed and reported by Administrator and/or Contracting Payor to the extent required under applicable Law; and (b) Administrator and/or Contracting Payor will disclose to each Qualified Health Plan, Exchange, or CMS the amount of Rebates received under this Agreement in the form and manner and to the extent required under applicable Law.

4.6.2 The parties intend that: (i) the Rebates qualify for safe harbor protection pursuant to the "Discount Safe Harbor," 42 C.F.R. 1001.952(h)(the "Discount Safe Harbor"); and (ii) the Administrative Fees qualify for safe harbor protection pursuant to the "GPO Safe Harbor," 42 C.F.R. 1001.952(j).

4.6.2.1 Manufacturer understands that Administrator's agreements with Contracting Payors may require Administrator to share some or all of the Administrative Fees with Contracting Payors.

7. Section 7.6 of the Agreement, "Notices," is hereby deleted in its entirety and replaced by the following new Section 7.6:

7.6 Notices. Except as set forth in Sections 2.1, 2.2, 3.2, 3.3 or as otherwise specified elsewhere in this Agreement, any notice required to be given under this Agreement shall be in writing and shall be deemed to have been duly given: (i) when delivered, if sent by United States registered or certified mail (return receipt requested); (ii) when delivered, if delivered personally by commercial courier; or (iii) on the second following business day, if sent by United States Express Mail, Federal Express or other commercial overnight courier, in each case to the following address (or at such other address as shall be specified by like notice) with applicable postage or delivery charges prepaid:

If to Administrator:
OptumRx, Inc.
17900 Von Karman Avenue, M/S CA016-0202
Irvine, CA 92614
Attn: S.V.P., Industry Relations

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With a copy to:
OptumRx, Inc.
2300 Main Street
M/S CA134-0507
Irvine, CA 92614
Attn: Industry Relations Legal Support

If to Manufacturer:
sanofi-aventis
Attention: Director, Contract Development
55 Corporate Drive
Mail Code 55B-300 US Market Access
Bridgewater, NJ 08807

With a copy to:
sanofi-aventis
Attention: Vice President and General Counsel
55 Corporate Drive
Mail Code 55A-525
Bridgewater, NJ 08807.

8. Exhibit A of the Agreement is hereby deleted in its entirety and replaced with the following new Exhibit A attached hereto.

9. Exhibit D of the Agreement is hereby deleted in its entirety and replaced with the following new Exhibit D attached hereto.

IN WITNESS WHEREOF the parties have caused this Amendment to be executed by their duly authorized officers or representatives as of the date first set forth above.

OptumRx, Inc.	**sanofi-aventis U.S. LLC**
By: [signature]	By: [signature]
Print Name: Kent Rogers	Print Name: Simon Jacot Guillarmod
Print Title: SVP, Industry Relations	Print Title: LEAD, CONTRACT DEVELOPMENT
Date: 9.21.18	Date: 10/03/2018

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EXHIBIT A
REBATE AND ADMINISTRATIVE FEE SCHEDULE

The terms and conditions in this Exhibit A are in addition to those Rebate terms and conditions otherwise set forth in Section 3.1.1 of the Agreement.

1. Definitions

1.1 Benefit Design

i. "Covered" means a Benefit design that does not qualify as a Managed or Highly Managed Benefit design.

ii. "Managed" means a Benefit design characterized by a Formulary under which the Contracting Payor directly or indirectly influences availability, or gives preference in dispensing decisions, of Drugs in one or more of the pharmaceutical categories serviced by such Formulary through (a) monetary restrictions (e.g., differential dollar Consumer co-payments for generic, branded Preferred and branded non-Preferred status as defined and determined by the Contracting Payor, where branded non-Preferred Drugs and branded Preferred Drugs have no less than an average co-payment differential of ten dollars ($10.00), or a co-insurance percentage differential), or (b) prior authorizations, NDC locks, step edits, or other similar mechanisms where certain Drugs are intended to be more restricted in availability than other Drugs.

iii. "Highly Managed" means a Benefit design characterized by a Formulary under which a Contracting Payor directly or indirectly influences availability, or gives preference in dispensing decisions, of Drugs in a significant portion of the pharmaceutical categories serviced by such Formulary through prior authorizations, NDC locks, step edits, or other similar mechanisms where certain Drugs are intended to be more restricted in availability than other Drugs.

1.2 "Formulary Status" means the position a Manufacturer Drug has on Formulary. A Formulary Status that is designated as 1 of [X] means that the Manufacturer Drug is 1 of [X] single-source brand name Drugs in the Defined Drug Market with the applicable Formulary Status; provided that for the purpose of determining if this condition for Rebate has been met, line extensions of Drugs within the Manufacturer Drug's Defined Drug Market manufactured by the same manufacturer shall be considered as one Drug [redacted]

1.3 "Preferred" means (i) a Drug is covered by a Benefit and is adjudicated on the Formulary tier that has the lowest co-payment amount or co-insurance percentage for brand name Drugs for the applicable Defined Drug Market and where the co-payment amount or co-insurance percentage for such Drug is lower than that of Drugs in the Defined Drug Market designated as "non-preferred", or (ii) a Drug is covered by a Benefit where the Drugs designated as "preferred" are covered by the Benefit and the Drugs excluded from Formulary or designated on Formulary as "non-preferred" or "excluded" are not covered by the Benefit or (iii) for Covered Benefit designs only, a Drug is covered by a Benefit

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where Drugs designated as "preferred" are covered by the Benefit and Manufacturer Drug is no more restricted in its availability than other brand name Drugs in the same Defined Drug Market.

1.4 "Specialty Tier" means a separate category or tier of the Formulary designated for very high cost or unique Drugs.

1.5 "Unrestricted Access" when referring to Lantus means a Manufacturer Drug is covered by a Benefit with no Utilization Controls, except for the allowances under the conditions to Rebates in Exhibit A. But when referring to all other Manufacturer Drugs, means a Manufacturer Drug covered by a Benefit with no Utilization Controls, except for the allowances set forth in 1.26 Utilization Controls in Article 1.

2. Rebate Calculation

Rebates for each Manufacturer Drug will be based upon the Formulary status of the Manufacturer Drug as of the date the Manufacturer Drug is dispensed. Rebates will be calculated on a per Unit dispensed basis. For each month, the Rebates for each Manufacturer Drug shall be calculated as follows:

Rebate = (Unit(s) of Manufacturer Drug) x (WAC) x (Total Rebate Rate for the applicable Manufacturer Drug)

3. Administrative Fee

The Administrative Fee rate is 4.75% for each Rebate eligible Unit of Manufacturer Drug. The Administrative Fee shall not be charged on QRPDP, Managed Medicaid and CHIP utilization, and any other utilization where prohibited by Law. With respect to any Administrative Fees paid by Manufacturer to Administrator, Administrator has informed Manufacturer that it will not agree not to pass through the Administrative Fee. Accordingly, Manufacturer will comply with the Discount Safe Harbor and recognize these as discounts in its federal price reporting. For each month, the Administrative Fee shall be calculated as follows:

Administrative Fee = (Unit(s) of Manufacturer Drug) x (WAC) x (Administrative Fee rate %)

4. Protection of Rebate Amount.

4.1 Price Protection

This Section 4.1 pertains to all Manufacturer Drugs except (a) where the "Price Protection factor" is denoted by "n/a" in the applicable Rebate tables in Sections 5, 6, 7, and 8 of Exhibit A of the Agreement or (b) those Manufacturer Drugs covered in Section 4.2 of Exhibit A of the Agreement.

i. Rebate rates are subject to automatic adjustment in the event the WAC per Unit for Manufacturer Drug exceeds the "Allowed WAC per Unit".

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ii. The initial "Allowed WAC per Unit" for a Manufacturer Drug is calculated by multiplying the WAC per Unit as of the date set forth in the Rebate terms below ("Baseline WAC Date") for the applicable Manufacturer Drug by (100% plus the "Price Protection" factor). The "Price Protection" factor is set forth in the Rebate terms below for the applicable Manufacturer Drug.

iii. The initial Allowed WAC per Unit for a Manufacturer Drug will apply during the "Initial Price Protection Period". The "Initial Price Protection Period" is defined as the 12-month period, or such other initial time period when indicated in the Rebate terms below, following such Manufacturer Drug's Price Protection Year Start Date, which date is set forth in the Rebate terms below. The applicable Manufacturer Drug's "Price Protection Year" is defined individually as the "Initial Price Protection Period" and each subsequent 12-month period.

iv. The "Base Rebate Rate %" is the then-current Rebate percentage for the Manufacturer Drug set forth in the Rebate tables below.

v. The "Allowed WAC per Unit" for subsequent Price Protection Years is calculated by multiplying the "Allowed WAC per Unit" for the previous Price Protection Year by (100% plus the "Price Protection" factor).

vi. The "Net WAC per Unit" is calculated by multiplying the WAC per Unit by (100% minus the Base Rebate Rate %).

vii. The "Net Allowed WAC per Unit" is calculated by multiplying the "Allowed WAC per Unit" by (100% minus the Base Rebate Rate %).

viii. Effective as of the date the WAC per Unit first exceeds the "Allowed WAC per Unit" and continuing for the remainder of that "Price Protection Year", subject to further adjustments in accordance with this Section 4.1 of this Exhibit A Rebate and Administrative Fee Schedule, an "Additional Rebate Rate" will be paid.

ix. The "Additional Rebate Rate" is calculated by determining the amount, if any, that the "Net WAC per Unit", in effect at the time the applicable Manufacturer Drug is dispensed, exceeds the "Net Allowed WAC per Unit" in effect at the time the applicable Manufacturer Drug is dispensed, divided by the then-current WAC per Unit.

x. The resulting percentage is the "Additional Rebate Rate" and is added to the "Base Rebate Rate %" to produce a "Total Rebate Rate" that applies to such utilization. For avoidance of doubt, the "Total Rebate Rate" calculation is subject to the terms of Section 2.2.6 Best Price in Article 2 except where otherwise indicated in this Exhibit A.

*The term "Net Allowed WAC" is used herein solely to explain the calculation of price protection in this Agreement. This term is not used outside of this Agreement and, furthermore, is not meant to define or describe any pricing terms of a Manufacturer Drug.

EXAMPLE 1:

	Assumed WAC as of 12/31/2013	Jan. 2014	Feb. 2014	Mar. 15 2014		Dec. 2014		Jan. 2015	Feb. 2015	Mar. 2015		Dec. 2015		Jan. 2016	Feb. 2016	Mar. 2016		Dec. 2016
Price Protection factor	6%			Year 1 Price increase 10%						Year 2 Price increase 10%						Year 3 Price increase 10%		
Current WAC/ Unit (Existing NDC)	6.00	6.00	6.00	6.60	→	6.60		6.60	6.60	7.26	→	7.26		7.26	7.26	7.99	→	7.99
Allowed WAC/ Unit (Existing NDC)		6.36	6.36	6.36		6.36	→	6.74	6.74	6.74		6.74	→	7.15	7.15	7.15		7.15
Current WAC/ Unit (New NDC)									6.60	7.26	→	7.26		7.26	7.26	7.99	→	7.99
Allowed WAC/ Unit (New NDC)									6.74	6.74		6.74	→	7.15	7.15	7.15		7.15
Current Net WAC / Unit		5.40	5.40	5.94		5.94		5.94	5.94	6.53		6.53		6.53	6.53	7.19		7.19
Net Allowed WAC / Unit	5.40	5.72	5.72	5.72		5.72		6.07	6.07	6.07		6.07		6.43	6.43	6.43		6.43
Additional Rebate		$0.00	$0.00	$0.22		$0.22		$0.00	$0.00	$0.47		$0.47		$0.10	$0.10	$0.76		$0.76
Additional Rebate Rate		0.0%	0.0%	3.3%		3.3%		0.0%	0.0%	6.4%		6.4%		1.4%	1.4%	9.5%		9.5%
Base Rebate Rate %	10.0%	10.0%	10.0%	10.0%		10.0%		10.0%	10.0%	10.0%		10.0%		10.0%	10.0%	10.0%		10.0%
Total Rebate Rate	10.0%	10.0%	10.0%	13.3%	→	13.3%		10.0%	10.0%	16.4%	→	16.4%		11.4%	11.4%	19.5%	→	19.5%

If a New NDC is introduced in the market after the date that such Manufacturer Drug becomes covered by this Agreement, the Additional Rebate Rate for such New NDC(s) will be calculated consistent with the preceding paragraph except that (i) the Net Allowed WAC per Unit for the Existing NDCs (defined below) will apply to the New NDC(s) during each billing period and (ii) the Net WAC per Unit of such New NDC(s) will be adjusted to account for differences, if any, in days of therapy, unit size, strength, or similar factors, between the New NDC(s) and their corresponding Existing NDCs, which adjustment(s) the parties will work in good faith to establish. As used herein, the term "Existing NDCs" refers to the Manufacturer Drug NDC(s) covered by the Agreement on the day prior to the date that the applicable New NDC comes into existence that has the highest Net Allowed WAC per Unit; provided, however, that either party may elect for the Existing NDC to be the NDC that most closely resembles the New NDC with respect to days of therapy, unit size, strength, or similar factors, which the parties will mutually determine working together in good faith. Example 2 below demonstrates the Additional Rebate Rate calculation for a New NDC

EXAMPLE 2:

New NDC introduced Feb14, subject to same PP rate increase as current NDCs
New NDC WAC normalized to Current NDC WAC, same Baseline WAC date
Price Protection factor: 6%

	Assumed WAC as of 12/31/2012	Jan. 2013	Feb. 2013	Mar. 15 2013 (Year 1 Price increase 10%)	Dec. 2013	Jan. 2014	Feb. 2014	Mar. 2014 (Year 2 Price increase 10%)	Dec. 2014	Jan. 2015	Feb. 2015	Mar. 2015 (Year 3 Price increase 10%)	Dec. 2015
Current WAC/ Unit (Current NDC)	6.00	6.00	6.00	6.60	6.60	6.60	6.60	7.26	7.26	7.26	7.26	7.99	7.99
Allowed WAC/ Unit (Current NDC)		6.36	6.36	6.36	6.36	6.74	6.74	6.74	6.74	7.15	7.15	7.15	7.15
Current WAC/ Unit (New NDC)							10.50	11.55	11.55	11.55	11.55	12.71	12.71
Current Normalized WAC/ Unit (New NDC)							9.90	10.89	10.89	10.89	10.89	11.98	11.98
Allowed WAC/ Unit (New NDC)							10.11	10.11	10.11	10.72	10.72	10.72	10.72
Current Net WAC / Unit (Current NDC)		5.40	5.40	5.94	5.94	5.94	5.94	6.53	6.53	6.53	6.53	7.19	7.19
Net Allowed WAC / Unit (Current NDC)	5.40	5.72	5.72	5.72	5.72	6.07	6.07	6.07	6.07	6.43	6.43	6.43	6.43
Current Net WAC / Unit (New NDC)							9.45	10.40	10.40	10.40	10.40	11.43	11.43
Net Allowed WAC / Unit (New NDC)							9.10	9.10	9.10	9.65	9.65	9.65	9.65
Additional Rebate (Current NDC)		$0.00	$0.00	$0.22	$0.22	$0.00	$0.00	$0.47	$0.47	$0.10	$0.10	$0.76	$0.76
Additional Rebate Rate (Current NDC)		0.0%	0.0%	3.3%	3.3%	0.0%	0.0%	6.4%	6.4%	1.4%	1.4%	9.5%	9.5%
Additional Rebate (New NDC)							$0.35	$1.29	$1.29	$0.75	$0.75	$1.79	$1.79
Additional Rebate Rate (New NDC)							3.3%	11.2%	11.2%	6.5%	6.5%	14.1%	14.1%
Base Rebate Rate %	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%
Total Rebate Rate (Current NDC)	10.0%	10.0%	10.0%	13.3%	13.3%	10.0%	10.0%	16.4%	16.4%	11.4%	11.4%	19.5%	19.5%
Total Rebate Rate (New NDC)							13.3%	21.2%	21.2%	16.5%	16.5%	24.1%	24.1%

	Current WAC	DOT (can be changed to whatever the 'normalization' factor should be)	Normalized WAC / per DOT	WAC in effect for New NDC
Current NDC	6.60	60	0.11	
New NDC	10.50	90		9.90

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4.2 Price Protection

This Section 4.2 pertains to the following Manufacturer Drugs with respect to the applicable Sections noted below in this Exhibit A:

[redacted]

Soliqua under Section 7.6

i. Rebate rates are subject to automatic adjustment in the event the WAC per Unit for a Manufacturer Drug exceeds the "Allowed WAC per Unit".

ii. The initial Allowed WAC per Unit" for a Manufacturer Drug is calculated by multiplying the WAC per Unit as of the date set forth in the Rebate terms below ("Baseline WAC Date") for the applicable Manufacturer Drug by (100% plus the "Price Protection" factor). The "Price Protection" factor is set forth in the Rebate terms below for the applicable Manufacturer Drug.

iii. The initial "Allowed WAC per Unit" for a Manufacturer Drug will apply during the "Initial Price Protection Period". The "Initial Price Protection Period" is defined as the 12-month period, or such other initial time period when indicated in the Rebate terms below, following such Manufacturer Drug's Price Protection Year Start Date, which date is set forth in the Rebate terms below. The applicable Manufacturer Drug's "Price Protection Year" is defined individually as the "Initial Price Protection Period" and each subsequent 12-month period.

iv. The "Base Rebate Rate %" is the then-current Rebate percentage for the Manufacturer Drug set forth in the Rebate tables below.

v. The "Allowed WAC per Unit" for Price Protection Years after the Initial Price Protection Period is calculated by multiplying the WAC per Unit as of December 31 of the immediately preceding calendar year by (100% plus the "Price Protection" factor).

vi. The "Net WAC per Unit" is calculated by multiplying the WAC per Unit by (100% minus the Base Rebate Rate %).

vii. The "Net Allowed WAC per Unit" is calculated by multiplying the "Allowed WAC per Unit" by (100% minus the Base Rebate Rate %).

viii. Effective as of the date the WAC per Unit first exceeds the "Allowed WAC per Unit" and continuing for the remainder of that "Price Protection Year", subject to further adjustments in accordance with this Section 4.2 of this Exhibit A Rebate and Administrative Fee Schedule, an "Additional Rebate Rate" will be paid. The "Additional Rebate Rate" is calculated by determining the amount, if any, that the "Net WAC per Unit", in effect at the time the applicable Manufacturer Drug is dispensed, exceeds the "Net Allowed WAC per Unit" in effect at the time the applicable Manufacturer Drug is dispensed, divided by the then-current WAC per Unit.

ix. The resulting percentage is the "Additional Rebate Rate" and is added to the "Base Rebate Rate %" to produce a "Total Rebate Rate" that applies to such utilization. For avoidance of doubt, the "Total Rebate Rate" calculation is subject to the terms of Section 2.2.6 Best Price in Article 2. Notwithstanding the above,

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the aggregate payment (Total Rebate Rate plus Administrative Fee) for [redacted] shall not exceed twenty-three percent (23%).

*The term "Net Allowed WAC" is solely used for purposes to explain the calculation of price protection in this Agreement. This term is not used outside of this Agreement and, furthermore, is not meant to define or describe any pricing terms of a Manufacturer Drug.

EXAMPLE 1:

Price Protection factor:	6%			Year 1 Price increase 10%				Year 2 Price increase 10%			
	Assumed WAC as of 12/31/2012	Jan. 2013	Feb. 2013	Mar. 15 2013	Dec. 2013	Jan. 2014	Feb. 2014	Mar. 2014	Dec. 2014	Jan. 2015	Feb. 2015
Current WAC/ Unit (Existing NDC)	6.00	6.00	6.00	6.60	6.60	6.60	6.60	7.26	7.26	7.26	7.26
Allowed WAC/ Unit (Existing NDC)		6.36	6.36	6.36	6.36	7.00	7.00	7.00	7.00	7.70	7.70
Current WAC/ Unit (New NDC)							6.60	7.26	7.26	7.26	7.26
Allowed WAC/ Unit (New NDC)							7.00	7.00	7.00	7.70	7.70
Current Net WAC / Unit		5.40	5.40	5.94	5.94	5.94	5.94	6.53	6.53	6.53	6.53
Net Allowed WAC / Unit	5.40	5.72	5.72	5.72	5.72	6.30	6.30	6.30	6.30	6.93	6.93
Additional Rebate :		$0.00	$0.00	$0.22	$0.22	$0.00	$0.00	$0.24	$0.24	$0.00	$0.00
Additional Rebate Rate:		0.0%	0.0%	3.3%	3.3%	0.0%	0.0%	3.3%	3.3%	0.0%	0.0%
Base Rebate Rate %:	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%
Total Rebate Rate	10.0%	10.0%	10.0%	13.3%	13.3%	10.0%	10.0%	13.3%	13.3%	10.0%	10.0%

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If a New NDC is introduced in the market after the date that such Manufacturer Drug becomes covered by this Agreement, the Additional Rebate Rate for such New NDC(s) will be calculated consistent with the preceding paragraph except that (i) the Net Allowed WAC per Unit for the Existing NDCs (defined below) will apply to the New NDC(s) during each billing period and (ii) the Net WAC per Unit of such New NDC(s) will be adjusted to account for differences, if any, in days of therapy, unit size, strength, or similar factors, between the New NDC(s) and their corresponding Existing NDCs, which adjustment(s) the parties will work in good faith to establish. As used herein, the term "Existing NDCs" refers to the Manufacturer Drug NDC(s) covered by the Agreement on the day prior to the date that the applicable New NDC comes into existence that has the highest Net Allowed WAC per Unit; provided, however, that either party may elect for the Existing NDC to be the NDC that most closely resembles the New NDC with respect to days of therapy, unit size, strength, or similar factors, which the parties will mutually determine working together in good faith. Example 2 below demonstrates the Additional Rebate Rate calculation for a New NDC.

EXAMPLE 2:

New NDC introduced Feb14, subject to same PP rate increase as Existing NDCs
Same WAC/unit, same Baseline WAC date
Price Protection factor 6%

	Assumed WAC as of 12/31/2012	Jan. 2013	Feb. 2013	Year 1 Price increase 10% Mar. 15 2013		Dec. 2013	Allowed was 6.74 Jan. 2014	Feb. 2014	Year 2 Price increase 10% Mar. 2014		Dec. 2014	Jan. 2015	Feb. 2015
Current WAC/ Unit (Existing NDC)	6.00	6.00	6.00	6.60	→	6.60	6.60	6.60	7.26	→	7.26	7.26	7.26
Allowed WAC/ Unit (Existing NDC)		6.36	6.36	6.36		6.36	7.00	7.00	7.00		7.00	7.70	7.70
Current WAC/ Unit (New NDC)								10.50	11.55	→	11.55	11.55	11.55
Current Normalized WAC/ Unit (New NDC)								9.90	10.89		10.89	10.89	10.89
Allowed WAC/ Unit (New NDC)								10.49	10.49		10.49	12.24	12.24
Current Net WAC / Unit (Existing NDC)		5.40	5.40	5.94		5.94	5.94	5.94	6.53		6.53	6.53	6.53
Net Allowed WAC / Unit (Existing NDC)	5.40	5.72	5.72	5.72		5.72	6.30	6.30	6.30		6.30	6.93	6.93
Current Net WAC / Unit (New NDC)								9.45	10.40		10.40	10.40	10.40
Net Allowed WAC / Unit (New NDC)								9.44	9.44		9.44	11.02	11.02
Additional Rebate (Existing NDC)		$0.00	$0.00	$0.22		$0.22	$0.00	$0.00	$0.24		$0.24	$0.00	$0.00
Additional Rebate Rate (Existing NDC)		0.0%	0.0%	3.3%		3.3%	0.0%	0.0%	3.3%		3.3%	0.0%	0.0%
Additional Rebate (New NDC)								$0.01	$0.95		$0.95	$0.00	$0.00
Additional Rebate Rate (New NDC)								0.1%	8.2%		8.2%	0.0%	0.0%
Base Rebate Rate %	10.0%	10.0%	10.0%	10.0%		10.0%	10.0%	10.0%	10.0%		10.0%	10.0%	10.0%
Total Rebate Rate (Existing NDC)	10.0%	10.0%	10.0%	13.3%	→	13.3%	10.0%	10.0%	13.3%	→	13.3%	10.0%	10.0%
Total Rebate Rate (New NDC)								10.1%	18.2%	→	18.2%	10.0%	10.0%

	Current WAC	DOT (can be changed to whatever the 'normalization' factor should be)	Normalized WAC / per DOT	WAC in effect for New NDC
Existing NDC	6.60	60	0.11	
New NDC	10.50	90		9.90

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5. **Rebate Terms – non-QRPDP, non-Managed Medicaid and non-CHIP.**

5.1 PREFERRED
5.1.1 Lantus: (Effective 1/1/2019 through 12/31/2022)

Manufacturer Drug Name: Lantus*				
Benefit Design	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 1 manufacturer with Preferred Drugs	75%	65%	50%
Base Rebate Rate %	1 of 2 manufacturers with Preferred Drugs	65%	50%	40%
Base Rebate Rate %	1 of 3 manufacturers with Preferred Drugs	n/a	n/a	26%
Administrative Fee		4.75%	4.75%	4.75%
Price Protection factor		4%	4%	4%
Baseline WAC Date		4/1/18	4/1/18	4/1/18
Price Protection Year Start Date		1/1/19	1/1/19	1/1/19

*The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, in Article 2 of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price in Article 2.

Conditions to Rebate For Rebate Table 5.1.1 Lantus:

1. Manufacturer Drug is Preferred and in the applicable Formulary Status in the table above; and
2. The following requirements apply to the corresponding Benefit designs noted below:

   (a) **For the Highly Managed Rebate,** Manufacturer is 1 of 1 or 1 of 2 manufacturer(s), as applicable, with Drug(s) in the Lantus Defined Drug Market that is(are) Preferred. All other manufacturers' Drugs in the Lantus Defined Drug Market that are non-Preferred satisfy one of the following: (i) they are not listed on Formulary and not covered, (ii) they are listed on Formulary but indicated as not covered, or (iii) if the Benefit design does not allow for a Drug to be excluded from Formulary as set forth in (i) and (ii), then they are listed and adjudicated on

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a Formulary tier with a higher co-payment amount or co-insurance percentage and are subject to a prior authorization or step edit through a Preferred Drug.

(b) **For the Managed Rebate**, Manufacturer is 1 of 1 or 1 of 2 manufacturer(s), as applicable, with Drug(s) in the Lantus Defined Drug Market that is(are) Preferred. All other manufacturers' Drugs in the Lantus Defined Drug Market that are non-Preferred satisfy one of the following: (i) they are listed and adjudicated on a Formulary tier with a higher co-payment amount or co-insurance percentage, (ii) they are not listed on Formulary and not covered, or (iii) they are listed on Formulary but indicated as not covered.

(c) **For the Covered Rebate**, Manufacturer is 1 of 1, 1 of 2 or 1 of 3 manufacturer(s), as applicable, with Drug(s) in the Lantus Defined Drug Market that is(are) Preferred. All other manufacturers' Drugs in the Lantus Defined Drug Market that are non-Preferred are either (i) listed and adjudicated on a Formulary tier with a higher co-payment amount or co-insurance percentage tier or (ii) not listed on Formulary.

3. Imposition of any of the following quantity limit requirements on Lantus will not render the applicable utilization ineligible for Rebates: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in the Lantus Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in the Lantus Defined Drug Market are subject to a quantity limit consistent with their respective package inserts; and
4. No package form of Lantus is disadvantaged to a comparable package form of any other Drug in the Lantus Defined Drug Market with regard to the applicable Benefit Contract's Utilization Controls. In the event that a package form of Lantus is disadvantaged to a comparable package form, all package forms of Lantus, i.e. both vial and pen, shall be ineligible for Rebates as of such date of dispensing. The following examples are provided for clarification of Rebate eligibility and not to be considered an exhaustive list:

Would Pay Vial and Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	1	Preferred	1	Preferred
Levemir	Vial	1	Preferred	1	Preferred
Lantus	Pen	1	Preferred	2	Preferred
Levemir	Pen	1	Preferred	2	Preferred

Would **NOT** Pay Vial or Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	1	Preferred	2	Preferred
Levemir	Vial	1	Preferred	1	Preferred
Lantus	Pen	3	Non-preferred	2	Preferred
Levemir	Pen	3	Non-preferred	2	Preferred

5.1.2 Apidra - (Effective 1/1/2019 through 12/31/2022)

Manufacturer Drug Name: Apidra				
Benefit Design	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 1	57%	57%	57%
Base Rebate Rate %	1 of 2	47%	47%	47%
Base Rebate Rate %	1 of 3	42%	42%	42%

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Administrative Fee		4.75%	4.75%	4.75%
Price Protection factor		n/a	n/a	n/a
Baseline WAC Date		n/a	n/a	n/a
Price Protection Year Start Date		n/a	n/a	n/a

Conditions to Rebate For Rebate Table 5.1.2 Apidra:

1. Manufacturer Drug is Preferred and in the applicable Formulary Status in the table above; and
2. The following requirements apply to the corresponding Formulary Status referenced in Rebate Table 5.1.2:
   (a) **For the 1 of 1 Formulary Status,** all other manufacturers' Drugs in the Apidra Defined Drug Market satisfy one of the following: (i) they are not listed on Formulary and not covered, (ii) they are listed on Formulary but indicated as not covered, or (iii) for Highly Managed Rebates only, if the Benefit design does not allow for a Drug to be excluded from Formulary as set forth in (i) and (ii), then they are listed and adjudicated on a Formulary tier with a higher co-payment amount or co-insurance percentage and are subject to a prior authorization or step edit through a Preferred Drug.
   (b) **For the 1 of 2 and 1 of 3 Formulary Status**, Manufacturer Drug is not disadvantaged as compared to other brand name Drugs in the Apidra Defined Drug Market with regard to the applicable Benefit Contract's Utilization Controls.
3. Imposition of any of the following quantity limit requirements on Apidra will not render the applicable utilization ineligible for Rebates: a quantity limit on Apidra that is: (i) no more than 70mls per month or 210mls per 3-month supply on Apidra vials and/or no more than 75mls per month or 225mls per 3-month supply on Apidra pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in the Apidra Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with Apidra's package insert provided all brand name Drugs in the Apidra Defined Drug Market are subject to a quantity limit consistent with their respective package inserts.

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5.1.5 Toujeo - (Effective 1/1/2019 through 12/31/2022)

Manufacturer Drug Name: Toujeo				
Benefit Design	Formulary Status	Highly Managed	Managed	Covered

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Base Rebate Rate %	1 of 1 manufacturers with Preferred Drugs	75%	65%	50%
Base Rebate Rate %	1 of 2 manufacturers with Preferred Drugs	65%	50%	40%
Base Rebate Rate %	1 of 3 manufacturers with Preferred Drugs	n/a	n/a	26%
Administrative Fee		4.75%	4.75%	4.75%
Price Protection factor		4.0%	4.0%	4.0%
Baseline WAC Date		4/1/18	4/1/18	4/1/18
Price Protection Year Start Date		1/1/19	1/1/19	1/1/19

Conditions to Rebate for Rebate Table 5.1.5 Toujeo:

1. Manufacturer Drug is Preferred and in the applicable Formulary Status in the table above; and
2. The following requirements apply to the corresponding Benefit designs noted below:
   - **(a)** **For the Highly Managed Rebate**, Manufacturer is 1 of 1 or 1 of 2 manufacturer(s), as applicable, with Drug(s) in the Toujeo Defined Drug Market that is(are) Preferred. All other manufacturers' Drugs in the Toujeo Defined Drug Market that are non-Preferred satisfy one of the following: (i) they are not listed on Formulary and not covered, (ii) they are listed on Formulary but indicated as not covered, or (iii) if the Benefit design does not allow for a Drug to be excluded from Formulary as set forth in (i) and (ii), then they are listed and adjudicated on a Formulary tier with a higher co-payment amount or co-insurance percentage and are subject to a step edit through a Preferred Drug.
   - **(b)** **For Managed Rebate,** Manufacturer is 1 of 1 or 1 of 2 manufacturer(s), as applicable, with Drug(s) in the Toujeo Defined Drug Market that is(are) Preferred. All other manufacturers' Drugs in the Toujeo Defined Drug Market that are non-Preferred satisfy one of the following: (i) they are listed and adjudicated on a Formulary tier with a higher co-payment amount or co-insurance percentage, (ii) they are not listed on Formulary and not covered, or (iii) they are listed on Formulary but indicated as not covered.
   - **(c)** **For Covered Rebate**, Manufacturer is 1 of 1, 1 of 2 or 1 of 3 manufacturers, as applicable, with Drug(s) in the Toujeo Defined Drug Market that is(are) Preferred. All other manufacturers' Drugs in the Toujeo Defined Drug Market that are non-Preferred are either (i) listed and adjudicated on a Formulary tier with

a higher co-payment amount or co-insurance percentage tier or (ii) not listed on Formulary; and

3. A Manufacturer Drug is not disadvantaged as compared to other brand name Drugs in the Toujeo Defined Drug Market with regard to the applicable Benefit Contract's Utilization Controls.
4. Imposition of any of the following quantity limit requirements on Toujeo will not render the applicable utilization ineligible for Rebates: (i) a quantity limit of no more than 225mls per 3-month supply on Toujeo provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in the Toujeo Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in the Toujeo Defined Drug Market are subject to a quantity limit consistent with their respective package inserts.

5.1.6 Soliqua 100/33 - (Effective 1/1/2019 through 12/31/2021)

Manufacturer Drug Name: Soliqua 100/33				
Benefit Design	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of many	42%	18%	10%
Administrative Fee		4.75%	4.75%	4.75%
Price Protection factor		0%	0%	0%
Baseline WAC Date		12/15/16	12/15/16	12/15/16
Price Protection Year Start Date		4/1/17	4/1/17	4/1/17

Conditions to Rebate for Rebate Table 5.1.6 Soliqua 100/33:

1. Manufacturer Drug is Preferred and in the applicable Formulary Status in the table; and
2. Manufacturer Drug is not disadvantaged as compared to other brand name Drugs in the Soliqua 100/33 Defined Drug Market with regard to the applicable Benefit Contract's Utilization Controls.
3. The parties acknowledge that the following step edit requirement on Soliqua 100/33 will not be deemed a disadvantage and will not render the applicable utilization ineligible for Rebates so long as such step edit requirement is applied to all other brand name Drugs in the Soliqua 100/33 Defined Drug Market where it is clinically appropriate to do so: Consumer has a history of trial of (i) at least one basal insulin Drug, or (ii) at least one GLP-1 Drug prior to Administrator or Contracting Payor providing coverage for Soliqua 100/33.

   Administrator and Contracting Payor acknowledge that (i) Manufacturer only endorses use of Soliqua 100/33 in accordance with its FDA approved prescribing information, a copy of which is available at the following internet address: http://products.sanofi.us/Soliqua 100/33/Soliqua_100-33.pdf, and (ii) to the extent required by applicable Law, Administrator's applicable internal advisory committees will review and approve step-edit criteria.

   Administrator or Contracting Payor, as applicable, will consider any Consumer who has filled any of the basal insulin or GLP-1 Drugs listed in the table below as having met the

step edit requirement listed in this section. A step edit that requires prior use of a specific basal insulin or GLP-1 Drug (as opposed to accepting any one of the Drugs in the table below) will render the applicable utilization ineligible for a Soliqua 100/33 Rebate.

Soliqua 100/33 Step Edit Requirement Table:

Basal Insulin*	GLP-1*
Lantus® Levemir® Tresiba® Basaglar® Toujeo® SoloSTAR® Toujeo® Max SoloSTAR®	Adlyxin® Bydureon® Byetta® Ozempic Tanzeum® Trulicity® Victoza®

*Other than Manufacturer Drugs that will be subject to section 2.4.1 in Article 2 of this Agreement, any new strengths, formulations and NDC numbers of the listed Drugs or addition of any new brand Drug will be added upon mutual written agreement of the parties, which agreement shall not be unreasonably withheld.

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6.1 PREFERRED

6.1.1 Lantus - (Effective 1/1/2019 through 12/31/2022):

Manufacturer Drug Name: Lantus*				
Benefit Design	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 1 manufacturers with Preferred Drugs	79.75%	69.75%	54.75%
Base Rebate Rate %	1 of 2 manufacturers with Preferred Drugs	69.75%	54.75%	44.75%
Base Rebate Rate %	1 of 3 manufacturers with Preferred Drugs	n/a	n/a	30.75%
Administrative Fee		n/a	n/a	n/a
Price Protection factor		4%	4%	4%
Baseline WAC Date		4/1/18	4/1/18	4/1/18
Price Protection Year Start Date		1/1/19	1/1/19	1/1/19

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, in Article 2 of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price in Article 2.

Conditions to Rebate For Rebate Table 6.1.1 Lantus:

1. Manufacturer Drug is Preferred and in the applicable Formulary Status in the table above; and
2. The following requirements apply to the corresponding Benefit designs listed below:
   (a) **For the Highly Managed Rebate,** Manufacturer is 1 of 1 or 1 of 2 manufacturer(s), as applicable, with Drug(s) in the Lantus Defined Drug Market that is(are) Preferred. All other manufacturers' Drugs in the Lantus Defined Drug Market that are non-Preferred satisfy one of the following: (i) they are not listed on Formulary and not covered, (ii) they are listed on Formulary but indicated as not covered, or (iii) if the Benefit design does not allow for a Drug to be excluded from Formulary as set forth in (i) and (ii), then they are listed and adjudicated on a Formulary tier with a higher co-payment amount or co-insurance percentage and are subject to a prior authorization or step edit through a Preferred Drug.

(b) **For the Managed Rebate**, Manufacturer is 1 of 1 or 1 of 2 manufacturer(s), as applicable, with Drug(s) in the Lantus Defined Drug Market that is(are) Preferred. All other manufacturers' Drugs in the Lantus Defined Drug Market that are non-Preferred satisfy one of the following: (i) they are listed and adjudicated on a Formulary tier with a higher co-payment amount or co-insurance percentage, (ii) they are not listed on Formulary and not covered, or (iii) they are listed on Formulary but indicated as not covered.

(c) **For the Covered Rebate**, Manufacturer is 1 of 1, 1 of 2 or 1of 3 manufacturer(s), as applicable, with Drug(s) in the Lantus Defined Drug Market that is(are) Preferred. All other manufacturers' Drugs in the Lantus Defined Drug Market that are non-Preferred are either (i) listed and adjudicated on a Formulary tier with a higher co-payment amount or co-insurance percentage or (ii) not listed on Formulary.

3. Imposition of any of the following quantity limit requirements on Lantus will not render the applicable utilization ineligible for Rebates: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in the Lantus Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in the Lantus Defined Drug Market are subject to a quantity limit consistent with their respective package inserts; and

4. No package form of Lantus will be disadvantaged to a comparable package form of any other Drug in the Lantus Defined Drug Market with regard to the applicable Benefit Contract's Utilization Controls. In the event that a package form of Lantus is disadvantaged to a comparable package form, all package forms of Lantus, both vial and pen, shall be ineligible for Rebates as of such date of dispensing. The following examples are provided for clarification of Rebate eligibility and not to be considered an exhaustive list:

Would Pay Vial and Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	1	Preferred	1	Preferred
Levemir	Vial	1	Preferred	1	Preferred
Lantus	Pen	1	Preferred	2	Preferred
Levemir	Pen	1	Preferred	2	Preferred

Would **NOT** Pay Vial or Pen

Product	Pkg Form	Tier	Status	Tier	Status
Lantus	Vial	1	Preferred	2	Preferred
Levemir	Vial	1	Preferred	1	Preferred
Lantus	Pen	3	Non-preferred	2	Preferred
Levemir	Pen	3	Non-preferred	2	Preferred

6.1.2 Apidra - (Effective 1/1/2019 through 12/31/2022)

Manufacturer Drug Name: Apidra				
Benefit Design	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of 1	61.75%	61.75%	61.75%
Base Rebate Rate %	1 of 2	51.75%	51.75%	51.75%
Base Rebate Rebate %	1 of 3	46.75%	46.75%	46.75%

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Administrative Fee		n/a	n/a	n/a
Price Protection factor		n/a	n/a	n/a
Baseline WAC Date		n/a	n/a	n/a
Price Protection Year Start Date		n/a	n/a	n/a

Conditions to Rebate For Rebate Table 6.1.2 Apidra:

1. Manufacturer Drug is Preferred and in the applicable Formulary Status in the table above; and
2. The following requirements apply to the corresponding Formulary Status referenced in Rebate Table 6.1.2:
   (a) **For the 1 of 1 Formulary Status**, all other manufacturers' Drugs in the Apidra Defined Drug Market satisfy one of the following: (i) they are not listed on Formulary and not covered, (ii) they are listed on Formulary but indicated as not covered, or (iii) for Highly Managed Rebates only, if the Benefit design does not allow for a Drug to be excluded from Formulary as set forth in (i) and (ii), then they are listed and adjudicated on a Formulary tier with a higher co-payment amount or co-insurance percentage and are subject to a prior authorization or step edit through a Preferred Drug.
   (b) **For the 1 of 2 and 1 of 3 Formulary Status**, Manufacturer Drug is not disadvantaged as compared to other brand name Drugs in the Apidra Defined Drug Market with regard to applicable Benefit Contract's Utilization Controls.
3. Imposition of the following quantity limit requirements on Apidra will not render the applicable utilization ineligible for Rebates: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Apidra vials and/or no more than 75mls per month or 225mls per 3-month supply on Apidra pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in the Apidra Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in the Apidra Defined Drug Market are subject to a quantity limit consistent with their respective package inserts.

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6.1.5 Toujeo - (Effective 1/1/2019 through 12/31/2022)

Manufacturer Drug Name: Toujeo				
Benefit Design	Formulary Status	Highly Managed	Managed	Covered

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Base Rebate Rate %	1 of 1 manufacturers with Preferred Drugs	79.75%	69.75%	54.75%
Base Rebate Rate %	1 of 2 manufacturers with Preferred Drugs	69.75%	54.75%	44.75%
Base Rebate Rate %	1 of 3 manufacturer with Preferred Drugs	n/a	n/a	30.75%
Administrative Fee		n/a	n/a	n/a
Price Protection factor		4.0%	4.0%	4.0%
Baseline WAC Date		4/1/18	4/1/18	4/1/18
Price Protection Year Start Date		1/1/19	1/1/19	1/1/19

Conditions to Rebate for Rebate Tables 6.1.5 Toujeo:

1. Manufacturer Drug is Preferred and in the applicable Formulary Status in the table above; and
2. The following requirements apply to the corresponding Benefit designs listed below:
   - **(a)** **For Highly Managed Rebate**, Manufacturer is 1 of 1 or 1 of 2 manufacturer(s), as applicable, with Drug(s) in the Toujeo Defined Drug Market that is(are) Preferred. All other manufacturers' Drugs in the Toujeo Defined Drug Market that are non-Preferred satisfy one of the following: (i) they are not listed on Formulary and not covered, (ii) they are listed on Formulary but indicated as not covered, or (iii) if Benefit design does not allow for a Drug to be excluded from Formulary as set forth in (i) and (ii), then they are listed and adjudicated on a Formulary tier with a higher co-payment amount or co-insurance percentage and are subject to a step edit through a Preferred Drug.
   - **(b)** **For Managed Rebate**, Manufacturer is 1 of 1 or 1 of 2 manufacturer(s), as applicable, with Drug(s) in the Toujeo Defined Drug Market that is(are) Preferred. All other manufacturers' Drugs in the Toujeo Defined Drug Market that are non-Preferred satisfy one of the following: (i) they are listed and adjudicated on a Formulary tier with a higher co-payment amount or co-insurance percentage, (ii) they are not listed on Formulary and not covered, or (iii) they are listed on Formulary but indicated as not covered.
   - **(c)** **For Covered Rebate**, Manufacturer is 1 of 1, 1 of 2 or 1 of 3 manufacturer(s), as applicable, with Drug(s) in the Toujeo Defined Drug Market that is(are) Preferred. All other manufacturers' Drugs in the Toujeo Defined Drug Market that are non-Preferred are either (i) listed and adjudicated on a Formulary tier with a higher co-payment amount or co-insurance percentage tier, or (ii) are not listed on Formulary; and

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3. Manufacturer Drug is not disadvantaged as compared to other brand name Drugs in the Toujeo Defined Drug Market with regard to the applicable Benefit Contract's Utilization Controls.
4. Imposition of any of the following quantity limit requirements on Toujeo will not render the applicable utilization ineligible for Rebates: (i) a quantity limit of no more than 225mls per 3-month supply on Toujeo provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in the Toujeo Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in the Toujeo Defined Drug Market are subject to a quantity limit consistent with their respective package inserts.

6.1.6 Soliqua 100/33 - (Effective 1/1/2019 through 12/31/2021)

Manufacturer Drug Name: Soliqua 100/33				
Benefit Design:	**Formulary Status**	**Highly Managed**	**Managed**	**Covered**
Base Rebate Rate %	1 of many	46.75%	22.75%	14.75%
Administrative Fee		n/a	n/a	n/a
Price Protection factor		0%	0%	0%
Baseline WAC Date:		12/15/16	12/15/16	12/15/16
Price Protection Year Start Date		4/1/17	4/1/17	4/1/17

Conditions to Rebate for Rebate Table 6.1.6 Soliqua 100/33:

1. Manufacturer Drug is Preferred and in the applicable Formulary Status in the table above; and
2. Manufacturer Drug is not disadvantaged as compared to other brand name Drugs in the Soliqua 100/33 Defined Drug Market with regard to the applicable Benefit Contract's Utilization Controls.
3. The parties acknowledge that the following step edit requirement on Soliqua 100/33 will not be deemed a disadvantage and will not render the applicable utilization ineligible for Rebates so long as such step edit requirement is applied to all other brand name Drugs in the Soliqua 100/33 Defined Drug Market where it is clinically appropriate to do so: Consumer has a history of trial of (i) at least one basal insulin Drug, or (ii) at least one GLP-1 Drug prior to Administrator or Contracting Payor providing coverage for Soliqua 100/33.

   Administrator and Contracting Payor acknowledge that (i) Manufacturer only endorses use of Soliqua 100/33 in accordance with its FDA approved prescribing information, a copy of which is available at the following internet address: http://products.sanofi.us/Soliqua 100/33/Soliqua 100-33.pdf, and (ii) to the extent required by applicable Law, Administrator's applicable internal advisory committees will review and approve step-edit criteria.

   Administrator or Contracting Payor, as applicable, will consider any Consumer who has filled any of the basal insulin or GLP-1 Drugs listed in the table below as having met the step edit requirement listed in this section. A step edit that requires prior use of a specific

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basal insulin or GLP-1 Drug (as opposed to accepting any one of the Drugs in the table below) will render the applicable utilization ineligible for a Soliqua 100/33 Rebate.

Soliqua 100/33 Step Edit Requirement Table:

Basal Insulin*	GLP-1*
Lantus® Levemir® Tresiba® Basaglar® Toujeo® SoloSTAR® Toujeo® Max SoloSTAR®	Adlyxin® Bydureon® Byetta® Tanzeum® Trulicity® Victoza®

*Other than Manufacturer Drugs that will be subject to section 2.4.1 in Article 2 of this Agreement, any new strengths, formulations and NDC numbers of the listed Drugs or addition of any new brand Drug will be added upon mutual written agreement of the parties, which agreement shall not be unreasonably withheld.

[redacted]

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[redacted]

7.6 **Soliqua 100/33- (Effective 1/1/2019 through 12/31/2021)**

Manufacturer Drug Name: Soliqua 100/33		
Benefit Design	**Formulary Status**	**Managed Medicaid**
Base Rebate Rate %	1 of 1	10%
Administrative Fee		n/a
Price Protection factor		9%
Baseline WAC Date		12/31/18
Price Protection Year Start Date		1/1/19

Conditions to Rebate for Rebate Table 7.6 Soliqua 100/33:

1. Manufacturer Drug is Preferred and in the applicable Formulary Status in the table above; and
2. All other Drugs in the Soliqua 100/33 Defined Drug Market are (a) in a non-Preferred Formulary tier or are non-Formulary and (b) subject to a step edit requiring trial and failure of all Preferred Drugs within the Soliqua 100/33 Defined Drug Market where it is clinically appropriate to so; and
3. Manufacturer Drug is not disadvantaged as compared to other brand name Drugs in the Soliqua 100/33 Defined Drug Market with regards to the applicable Benefit Contract's Utilization Controls; and
4. The parties acknowledge that the following step edit requirement on Soliqua 100/33 will not be deemed a disadvantage and shall not render the applicable utilization ineligible for Rebates so long as such step edit requirement is applied to all other brand name Drugs in the Soliqua 100/33 Defined Drug Market where it is clinically appropriate to do so: (i) Consumer has a history of trial of (i) at least one basal insulin Drug, or (ii) at least one GLP-1 Drug prior to Administrator or Contracting Payor providing coverage for Soliqua 100/33.

Administrator and Contracting Payor acknowledge that (i) Manufacturer only endorses use of Soliqua 100/33 in accordance with its FDA approved prescribing information, a copy of which is available at the following internet address: http://products.sanofi.us/Soliqua 100/33/Soliqua 100-33.pdf. and (ii) to the extent required by applicable Law, Administrator's applicable internal advisory committees will review and approve step-edit criteria.

Administrator will or Contracting Payor, as applicable will consider any Consumer who has filled any of the basal insulin or GLP-1 Drugs listed in the table below as having met the step edit requirement listed in this section. A step edit that requires prior use of a specific basal insulin or GLP-1 Drug (as opposed to accepting any one of the Drugs in the table below) will render the applicable utilization ineligible for a Soliqua 100/33 Rebate.

Soliqua 100/33 Step Edit Requirement Table:

Basal Insulin*	**GLP-1***
Lantus®	Adlyxin®
Levemir®	Bydureon®
Tresiba®	Byetta®
Basaglar®	Tanzeum®
Toujeo® SoloSTAR®	Trulicity®
Toujeo® Max SoloSTAR®	Victoza®

*Other than Manufacturer Drugs that will be subject to section 2.4.1 of this Agreement, any new strengths, formulations and NDC numbers of the listed Drugs or addition of any new brand Drug will be added upon mutual written agreement of the parties, which agreement shall not be unreasonably withheld.

[redacted]

[redacted]

7.8 (Effective 1/1/2019 through 12/31/2020)

Manufacturer Drug Name: Admelog®		
Benefit Design	**Managed Medicaid**	**Managed Medicaid**
Formulary Status	1 of 1 manufacturer	1 of 2 manufacturer
Base Rebate Rate % Admelog® Vials	15%	3%
Base Rebate Rate % Admelog® SoloSTAR®	15%	4%
Administrative Fee	n/a	n/a
Price Protection factor	8%	8%
Baseline WAC Date	3/12/18	3/12/18
Price Protection Year Start Date	4/1/18	4/1/18

Conditions to Rebates for Rebate Table 7.8 Admelog:

1. Manufacturer Drug is Preferred with Unrestricted Access and in the applicable Formulary Status in the table above; and
2. All other single source brand name Drugs in the Admelog Defined Drug Market are (a) in a non-Preferred Formulary tier or are non-Formulary and (b) where the Benefit design allows, subject to a step edit requiring trial of all Preferred Drugs within the Admelog Defined Drug Market, where it is clinically appropriate to do so; and
3. No package form of Admelog is disadvantaged to a comparable package form of any other single-source brand name Drug in the Admelog Defined Drug Market with regard to the applicable Benefit Contract's [redacted]tilization Controls. In the event a package form of Admelog is disadvantaged to a comparable package form, all package forms of Admelog, i.e. both vial and pen, shall be ineligible for Rebates as of the date of dispensing. Notwithstanding the foregoing, Admelog SoloSTAR may be subject to a step edit, requiring the trial of Admelog vials before the utilization of Admelog SoloSTAR. If Administrator, or Contracting Payor, as applicable, implement a medical exception to such

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[redacted]

8. **Rebate Terms – CHIP a stand-alone Federal healthcare program that operates independent from the Medicaid program as set forth in Article 2 Payment and Billing, Section 2.2.4.**

8.1 Lantus - (Effective 1/1/2019 through 12/31/2022)

Manufacturer Drug Name: Lantus*		
Benefit Design	**Formulary Status**	**CHIP**
Base Rebate Rate %	1 of 2 or fewer manufacturers with Preferred Drugs	69.75%
Administrative Fee		n/a
Price Protection factor		4%
Baseline WAC Date		4/1/18
Price Protection Year Start Date		1/1/19

* The Rebate and Administrative Fee terms set forth in the above table are not subject to Section 2.2.6, Best Price, in Article 2of this Agreement; under no circumstances will the Rebate and Administrative Fee obligations set forth in the above table be reduced or otherwise affected by the application of Section 2.2.6, Best Price in Article 2.

Conditions to Rebate for Rebate Table 8.1 Lantus:

1. Manufacturer is one (1) of two (2) or fewer manufacturers with Drug(s) in the Lantus Defined Drug Market that is(are) Preferred. All other manufacturers' Drugs are listed and adjudicated on a higher tier and are subject to a step edit through a Preferred Drug; and
2. Imposition of any of the following quantity limit requirements on Lantus will not rend the applicable utilization ineligible for Rebates: (i) a quantity limit of no more than 70mls per month or 210mls per 3-month supply on Lantus vials and/or no more than 75mls per month or 225mls per 3-month supply on Lantus pen provided there is an exception process for such quantity limit when an exception is medically necessary and all brand

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name Drugs in the Lantus Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in the Lantus Defined Drug Market are subject to a quantity limit consistent with their respective package inserts; and

3. No package form of Lantus will be disadvantaged to a comparable package form of any other Drug in the Lantus Defined Drug Market with regard to the applicable Benefit Contract's Utilization Controls. In the event that a package form of Lantus is disadvantaged to a comparable package form, all package forms of Lantus, i.e. both vial and pen, shall be ineligible for Rebates as of such date of dispensing.

[redacted]

[redacted]

8.5 Toujeo - (Effective 1/1/2019 through 12/31/2022)

Manufacturer Drug Name: Toujeo		
Benefit Design	**Formulary Status**	**CHIP**
Base Rebate Rate %	1 of 2 or fewer manufacturers	69.75%

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	with Preferred Drugs	
Administrative Fee		n/a
Price Protection factor		4%
Baseline WAC Date		4/1/18
Price Protection Year Start Date		1/1/19

Conditions to Rebate for Rebate Table 8.5 Toujeo:

1. Manufacturer is one (1) of two (2) or fewer manufacturers with Drug(s) in the Toujeo Defined Drug Market that is(are) Preferred. All other manufacturers' Drugs are listed and adjudicated on a Formulary tier with a higher co-payment amount or co-insurance percentage and are subject to a step edit through a Preferred Drug; and
2. Manufacturer Drug is not disadvantaged as compared to other brand name Drugs in the Toujeo Defined Drug Market with regard to the applicable Benefit Contract's Utilization Controls; and
3. Imposition of any of the following quantity limit requirements on Toujeo will not render the applicable utilization ineligible for Rebates: (i) a quantity limit of no more than 225mls per 3-month supply on Toujeo provided there is an exception process for such quantity limit when an exception is medically necessary and all brand name Drugs in the Toujeo Defined Drug Market are subject to the same quantity limit, or (ii) a quantity limit consistent with its package insert provided all brand name Drugs in the Toujeo Defined Drug Market are subject to a quantity limit consistent with their respective package inserts.

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8.13 (Effective 1/1/2019 through 12/31/2020)

Manufacturer Drug Name: Admelog®		
Benefit Design	**CHIP**	**CHIP**
Formulary Status	1 of 1 manufacturer	1 of 2 manufacturer
Base Rebate Rate % Admelog® Vials	15%	3%
Base Rebate Rate % Admelog® SoloSTAR®	15%	4%
Administrative Fee	n/a	n/a
Price Protection factor	8%	8%
Baseline WAC Date	3/12/18	3/12/18
Price Protection Year Start Date	4/1/18	4/1/18

Conditions to Rebates for Rebate Table 8.13 Admelog:

1. Manufacturer Drug is Preferred with Unrestricted Access and in the applicable Formulary Status in the table above; and
2. All other single-source brand name Drugs in the Admelog Defined Drug Market are (a) in a non-Preferred Formulary tier or are non-Formulary and (b) where the Benefit design allows, subject to a step edit requiring trial of all Preferred Drugs within the Admelog Defined Drug Market, where it is clinically appropriate to do so; and
3. No package form of Admelog is disadvantaged to a comparable package form of any other Drug in the Admelog Defined Drug Market with regard to the applicable Benefit Contract's Utilization Controls. In the event a package form of Admelog is disadvantaged to a comparable package form, all package forms of Admelog, i.e. both vial and pen, shall be ineligible for Rebates as of the date of dispensing. Notwithstanding the foregoing, Admelog SoloSTAR may be subject to a step edit, requiring the trial of Admelog vials before the utilization of Admelog SoloSTAR. If Administrator, or Contracting Payor, as applicable, implement a medical exception to such step edit that uses a prior authorization process to determine whether the step edit is medically appropriate, such prior authorization process will not be deemed disadvantaging for purposes of this Section 8.13(3).

EXHIBIT D

DEFINED DRUG MARKET

[redacted]

Apidra® Apidra® SoloSTAR® Admelog® Vials Admelog® SoloSTAR®	Fiasp Fiasp FlexTouch Humalog Humalog Kwik Pen / Junior KwikPen Novolog Novolog FlexPen Novolog FlexTouch

[redacted]

Lantus® Lantus® SoloSTAR® Toujeo® SoloSTAR®	Basaglar KwikPen Levemir Levemir FlexTouch

MANUFACTURER DRUG	COMPETITIVE DRUG
Toujeo® Max SoloSTAR®	Tresiba FlexTouch
[redacted]	
Apidra® Apidra® SoloSTAR® Admelog® Vials Admelog® SoloSTAR®	Fiasp Fiasp FlexTouch Humalog Humalog Kwik Pen / Junior KwikPen Novolog Novolog FlexPen Novolog FlexTouch
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	Lantus® Lantus® SoloSTAR® Toujeo® SoloSTAR® Toujeo® Max SoloSTAR®	<u>Insulin</u> Basaglar KwikPen Humalog Mix 50/50 Humalog Mix 50/50 KwikPen Humalog Mix 75/25 Humalog Mix 75/25 KwikPen Humulin 70/30 Humulin 70/30 KwikPen Humulin N Humulin N KwikPen Levemir Levemir FlexTouch Novolin 70/30 Novolin N Novolin Mix 70/30 Novolin Mix 70/30 FlexPen Relion Mix 70/30 Relion N Ryzodeg 70/30 Tresiba FlexTouch	[redacted]

[redacted]

[redacted]

Response to Request No. 9.a:

OptumRx reimburses its network pharmacies for insulin that they dispense to members based on the terms of the specific agreements that OptumRx enters with each pharmacy. Generally, under OptumRx's agreements with network pharmacies, the reimbursement rates to pharmacies are calculated as the lesser of: (i) a specified percentage discount to the average wholesale price ("AWP"), as defined in each agreement, (ii) the pharmacy's usual and customer ("U&C") charge for the drug, or (iii) the Maximum Allowable Cost ("MAC") for certain generic drugs and brand drugs with generic alternatives managed on a MAC list. These reimbursement rates are not separately defined or negotiated for dispensing insulin as compared to other pharmaceuticals.

OptumRx reimburses its network pharmacies at competitive rates that balance compensating pharmacies fairly with providing an affordable benefit for clients and members. While OptumRx is not privy to the rates at which any given pharmacy purchases drugs, OptumRx consults a variety of independent data sources in an effort to reimburse pharmacies at competitive rates that exceed network pharmacies' overall acquisition costs.

Response to Request No. 9.b:

Maximum Allowable Cost ("MAC") pricing applies to certain generic drugs or brand name drugs with generic versions. OptumRx typically does not use a MAC list in connection with insulin products, which do not currently have generic versions.

Response to Request No. 9.c:

OptumRx works with highly sophisticated clients who choose how they prefer to compensate OptumRx for the pharmacy care services that OptumRx provides. OptumRx supports client choice and offers clients the option of contracting under a traditional, or "spread," pricing structure. Clients that choose a traditional pricing structure accounted for slightly less than 20 percent of OptumRx's total claims volume from 2016 through 2018. However, in the commercial sector, OptumRx continues to see many of its clients choose this type of arrangement. For example, in 2019 roughly 60% of OptumRx's largest commercial clients elected a traditional pricing arrangement. Under a traditional pricing structure, the client negotiates a contracted rate with OptumRx for drugs, irrespective of what OptumRx has contracted to pay the pharmacy. For a client that chooses a traditional model, OptumRx bears the risk that it can negotiate a rate with the pharmacy that is below the cost it has contracted with the client. Some clients do not want to assume the financial risks and potential financial uncertainty of a pass-through pricing structure and instead prefer risk-based contracting approaches, like a traditional pricing structure, which provide financial certainty and incentivizes performance and value.

As discussed in previous responses, OptumRx does not, in the ordinary course of business, calculate the annual gross profit per claim for insulin products or other drugs, because its costs and revenues are not typically allocated to particular drugs, classes of drugs, or claims. As a provider of pharmacy care services, OptumRx provides a wide range of interrelated services to its clients, including clinical services, formulary design, rebate negotiation, claims administration, claims adjudication, pharmacy network management, and home delivery pharmacy operations, among others. Many of these services result in revenues and costs that are not readily allocated on the basis of a particular transaction, drug, class of drugs, or prescription claim.

Response to Request No. 9.d:

OptumRx supports client choice and offers clients the option of contracting under a pass-through pricing structure. Clients that choose pass-through pricing structures accounted for more than 80 percent of OptumRx's total claims volume from 2016 through 2018. Under a pass-through pricing structure, the client pays OptumRx what OptumRx pays the pharmacy for every dispensed prescription.

As discussed in response to Request No. 9.c, OptumRx does not, in the ordinary course of business, calculate the annual gross profit per claim for insulin products or other drugs.

Supplemental Response to Request No. 3:

As described in OptumRx's previous responses, OptumRx's Industry Relations group negotiates contracts and discounts with drug manufacturers, including manufacturers of insulin. Numerous individuals are involved in these negotiations, but Lisa Erickson and Kent Rogers have primary leadership responsibility. OptumRx representatives have periodic discussions with insulin manufacturers concerning overall pricing issues. In the course of those discussions, OptumRx continually seeks to obtain the lowest possible net cost for its customers and consumers, regardless of the list prices set by the manufacturers.

OptumRx's Formulary Management Committee ("FMC") has the authority to make decisions regarding the placement of prescription drugs on OptumRx's standard formularies. Subject to the clinical designations and recommendations of the Pharmacy & Therapeutics ("P&T") Committee, the FMC considers the availability of rebates in making formulary placement decisions.

Standard formularies are available online and are viewable by members, clients, and partners in the supply chain. In addition, all formulary placement changes are communicated in advance of their effective dates to clients and members whose claims may be affected. OptumRx provides supporting documentation regarding its formulary recommendations if such information is requested and provided under the terms of the client's contract. Manufacturers are notified of formulary placement changes by an OptumRx Industry Relations business lead.